# The Journal of Laboratory and Clinical Medicine

VOL. VII ST. LOUIS, APRIL, 1922 NO. 7


## ORIGINAL ARTICLES

### THE NERVOUS CONTROL OF THE PYLORIC SPHINCTER*


BY J. EARL THOMAS, M.D., ST. LOUIS, MO., AND HOMER WHEELON, M.D., SEATTLE, WASH.


ACCORDING to the theories of the function of the pyloric sphincter which have been prevalent until recently[1] this structure has been regarded as a separate functional entity subject to a special set of reflexes from the gastric and duodenal mucosa. Gaskell[2] deduced from his theories of development that the pyloric sphincter has a special nerve supply, different from that of the stomach and duodenum. A similar inference might be drawn from the idea that the pyloric function is distinct from that of the rest of the gastric muscle.

Recent work[3, 4, 5, 6, 7] has tended to discredit the idea of a special reflex control of the pyloric sphincter and to establish the view that all of the muscle of the pyloric portion of the stomach, including the sphincter, is a single functional unit. It is a logical deduction from these findings that all of the muscle of the pars pylorica should respond in a similar way to stimulation of its extrinsic nerve supply. The nervous physiology of the stomach has been studied extensively, that of pyloric sphincter less so; however, the results obtained demonstrate in a striking way the unity of the musculature of the pars pylorica in its relation to the extrinsic nerves. (In fact a much greater difference is to be observed between the responses of the fundic and pyloric portions of the stomach, than between the responses of the sphincter and the rest of the pars pylorica.)

#### REVIEW OF LITERATURE

Openchowski,[8] who gave us the first systematic study of the nervous control of the stomach considered the vagus nerve entirely motor to the pyloric


*From the Department of Physiology of the St. Louis University School of Medicine, St. Louis, Mo. Received for publication, August 3, 1921.

sphincter. Katz and Winkler,[9] Dixon,[10] and others also demonstrated motor responses in the pylorus following vagus stimulation. Peristaltic waves in the pylorus, according to Langley[11] are excited and augmented because of the reception of impulses over the vagi. It is evident from these findings that the pyloric sphincter receives excitatory fibers over the vagi. That the same is true for the remainder of the stomach is shown by the following:

According to Dixon[10] vagus excitation augments automatic contractions and increases gastric tonicity. Morat[12, 13] reports that stimulation of the central end of the severed splanchnic nerves causes contraction of the stomach. Section of the splanchnics in the frog Patterson[14] and dog Carlson[15] results in a hypertonic stomach, i.e., increased gastric tonus, and in the dog an augmentation of hunger contractions. Such hypertonicity following splanchnic section is interpreted as an unopposed bulbar activity over the vagus. On the other hand Carlson[15] states that section of the vagi leaves the empty stomach, on the whole, permanently hypotonic, at least for 3 months. Cannon[16, 17] reports that vagus section results in a temporary loss of gastric tonus and a slowing or weakening of the peristalsis. According to Pavlov[18] vagus section below the heart permits of the retention of food in the stomach and a deficiency of pyloric action. Food is not easily carried out of the stomach. Kelling[19] regards the vagi as excitors to gastric tension, the result of such tonic states being rhythmic contraction. According to Ducceschi[20] only one vagus nerve is required to give the entire surface of the stomach a motor supply.

The accepted function of the vagi on the small intestine is that of excitation of tonus and contraction.[2, 31, 32] The same uniformity is shown in the distribution of the inhibitory fibers of the vagus. The studies of Langley[11] led him to draw the conclusion that "the body of the stomach and pylorus receive inhibitory as well as motor fibers from the vagus." These conclusions were drawn from observations on atropinized cats and rabbits during vagus excitation. These results were confirmed for the pyloric sphincter by Page May,[21] who used graphic methods. Wertheimer[22] observed reflex inhibition of the stomach following stimulation of the central end of one vagus nerve, the other remaining intact. Stimulation of the central stump of the vagus when both nerves were cut did not result in as great a degree of inhibition. This author also states that stimulation of the central stump of the severed sciatic nerve resulted in gastric inhibition. Morat[13] also observed gastric inactivity following stimulation of the central end of a cut vagus. Dixon[10] working on frogs showed that stimulation of the vagus inhibited gastric tonus and augmented gastric contractions or movements. Auer[23] states that only a slight degree of reflex inhibition occurs through the vagi in rabbits.

In like manner no difference can be noted in the reported effects on the pyloric sphincter and other gastric muscle following splanchnic stimulation. Inhibition and excitation have both been observed. Elliott[24] found that the pyloric sphincter of the rabbit was contracted by adrenalin as well as by splanchnic stimulation. Openchowski[8] found the splanchnic mainly motor to the stomach and pyloric sphincter in rabbits, less so in dogs. According to Schiff[25]

motor fibers reach the stomach from the splanchnics by way of the solar plexus. Morat[12] held a similar view. Contegean[26] states that stimulation of the splanchnics in amphibians causes contraction, especially of the circular fibers. Courtade[27] also showed tonic contractions of the circular fibers of the stomach following splanchnic stimulation. However, this author states that inhibition of the longitudinal fibers occurs at the time of the contraction of the circular fibers. Waters[28] observed that strong stimulation of the 3rd, 4th, and 5th nerves of the frog at their exit from the spinal cord resulted in contractions of the stomach and at times of the duodenum. Steinach[29] made similar observations. Dixon[10] found that stimulation of the 3rd, 4th, and 5th nerves, especially of the 4th, resulted in increased gastric tone and lessened contractions after a latent period of about 8 seconds.

As to inhibition, Katz and Winkler[9] from their studies of the nervous supply of the stomach, conclude that the splanchnics cause the pylorus to open, i.e., to lose tone. Similar results were reported by Oser.[30] According to Auer[23] complete reflex inhibition of the stomach can be obtained only when the splanchnics are intact. Morat[12] found that stimulation of the sciatic nerve, or other sensory paths, at times resulted in a "splanchnic" (motor) effect on the stomach, at other times in a "vagal" (inhibition) effect. Patterson[14] observed on the frog that section of the vagi with the splanchnics left intact resulted in a hypotonic stomach. Cannon[16] states that section of the vagi results in an unopposed constant inhibitory action of the splanchnics which causes permanent disturbances of the gastric motor functions. Wertheimer[22] and also Openchowski[8] demonstrated gastric inhibition following splanchnic stimulation.

From the literature cited the conclusion may be drawn that the vagi and splanchnics both carry motor and inhibitory impulses to the stomach as a whole as well as to the pyloric sphincter. However, there is no direct evidence to show whether in a given case motor or inhibitory effects are obtained simultaneously on gastric wall and sphincter or if one is inhibited when the other contracts. In view of the complex nature of the nerve supply such evidence is necessary before inferences relative to the functional relation of these parts can reasonably be drawn from studies of the nervous physiology.

In the course of an investigation involving the application of graphic methods to the study of the motility of the antrum and pyloric sphincter and first part of the duodenum, advantage was taken of the opportunity to obtain simultaneous records showing the effect of stimulating the extrinsic nerves to these structures. In general the findings described in the preceding review of literature were confirmed. In addition the relation of the motor and inhibitory responses of the antrum and pyloric sphincter to each other and to those of the duodenum was observed as well as the effect of stimulation of the extrinsic nerves on the rhythmicity of the pyloric sphincter, a function which has not hitherto been studied. So far as we can learn the method of obtaining simultaneous graphic records such as we used has not been applied to the investigation of this subject. In fact graphic records of any sort showing

the effect of stimulating the extrinsic nerves to the stomach, and especially to the pyloric sphincter are extremely rare in the literature.

## EXPERIMENTAL METHODS

Our experiments were performed on dogs. In all 171 stimulations were done on 36 animals. Ether anesthesia was used for all operative procedures. In most cases ether was used throughout the experiment. In some cases morphine was used in addition to ether and in certain experiments morphine alone was relied upon after the operations were completed. The three methods of anesthesia gave similar results but the most satisfactory from every point of view was ether with a small dose of morphine.

The method of obtaining graphic records of the movements of the pars pylorica and duodenum has been described in detail in previous publications.[5, 6, 33] When the sphincter alone was to be studied a specially constructed balloon consisting of a finger cot stretched over two hard rubber

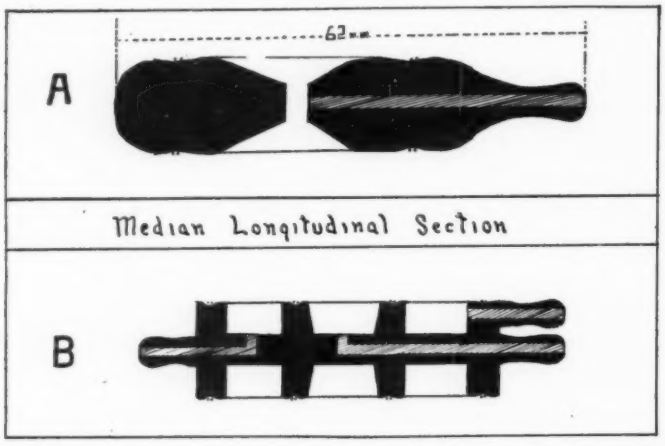


Fig. 1.—Diagram of apparatus; *A*, modified balloon or pylorograph; *B*, triple chambered balloon or triple enterogram used to record simultaneously contractions of the pyloric sphincter, antrum, and duodenum.

cones (Fig. 1*A*) was placed in the pyloric canal through an opening in the fundic end of the stomach and secured in place by sutures through the gastric and duodenal walls. When the pylorus antrum and first part of the duodenum were also to be studied a balloon divided into three parts was secured in position and a tube led from each portion so that simultaneous records could be made of antral, sphincteric, and duodenal contractions (Fig. 1*B*). Pressure was maintained in these balloons by means of a water manometer connected to each. Pressures in the chambers were varied according to our judgment of the tonus of the structures concerned. As a rule a slightly higher pressure was needed in the pyloric balloon than in the others. Pressures near 25 cms. of water were used most of the time. Registration was accomplished by means of a piston recorder for the pyloric records and bellows recorders for the other structures.

Stimulation was with the interrupted induced current from the secondary

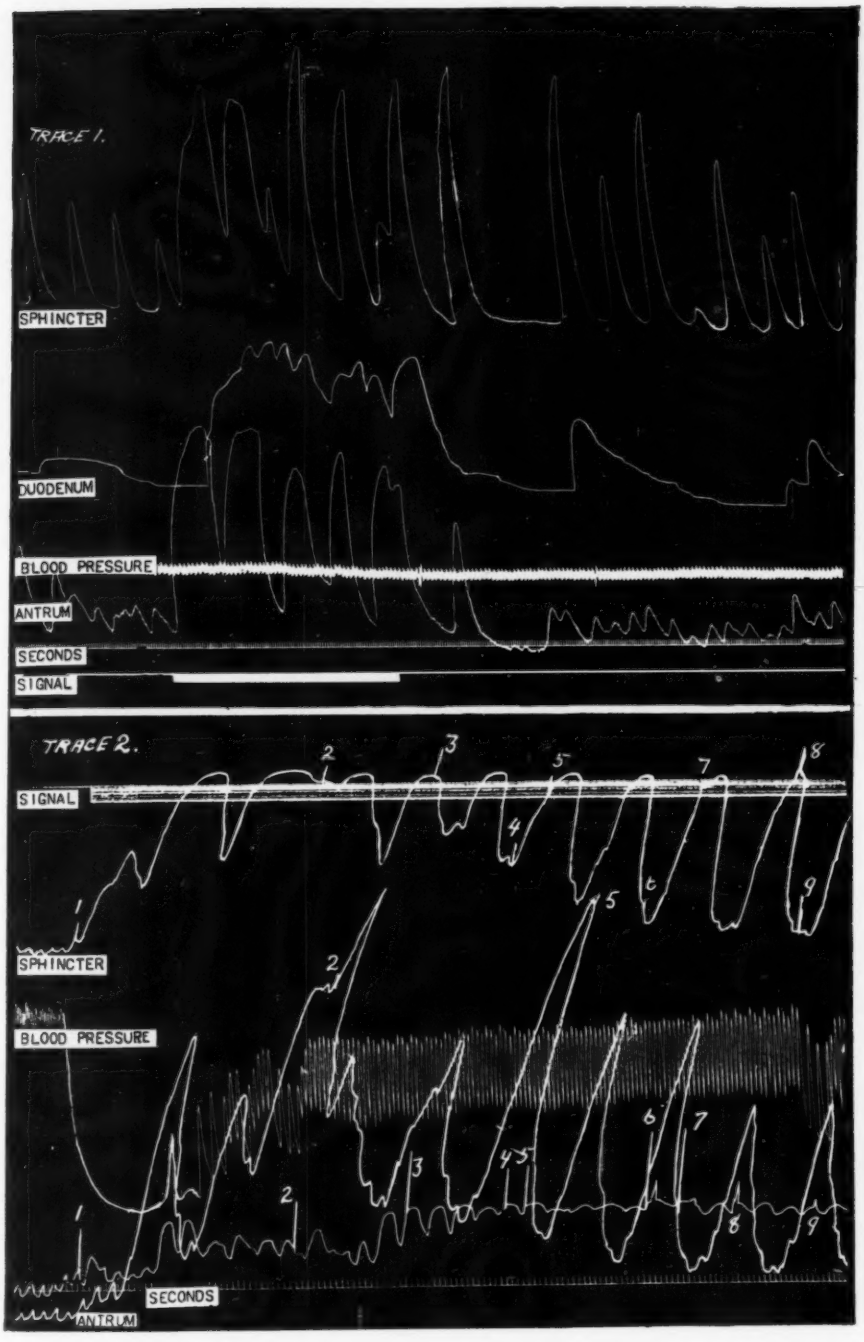


Fig. 2.—Enterograms showing the effect of vagus stimulation on the pyloric sphincter, antrum, and first part of the duodenum. Trace 1, experiment 23, February 7, 1920, ether used throughout the experiment. Vagus stimulated below the heart. Secondary coil at 9 cm. Trace 2, experiment 26, February 14, 1920, animal operated under ether, experiments conducted under the influence of sodium veronal. Vagus stimulated in the neck. Secondary of the Bois Raymond coil at 9 cm. Figures indicate synchronous points.

Note the similarity of the motor responses of the sphincter, antrum, and duodenum, also that the result is not affected by the marked circulatory disturbance, shown in trace 2.

of a Harvard or a Du Bois Raymond inductorium. The current was varied in strength according to the irritability of different preparations. In other respects it remained uniform. The primary current was obtained from a battery of storage cells connected in multiple.

In preparing the nerves for stimulation, when both the vagus and splanchnic were to be studied, a piece of one of the lower ribs was resected and both the vagi and one splanchnic, usually the left, secured and cut. The peripheral ends of the vagi were then placed in one electrode and the splanchnic in another. Electrodes of the Sherrington type were used. The thoracic incision was then closed around the wires (encased in rubber tubing), and made air-tight so that artificial respiration could be discontinued.

In many experiments we were mainly interested in the splanchnics and in these the nerves were secured below the diaphragm through a lateral incision parallel to the last rib and as near to it as possible. Frequently in these animals the vagi were picked up in the neck and stimulated. We recognize the theoretical objection to this method of vagus stimulation because of the effect it has on the circulation, nevertheless in practice the results were identical with those obtained from stimulation below the heart.

## EXPERIMENTAL RESULTS

1. *The Effect of Cutting the Nerves.*—It was necessary to cut one or more of the nerves in preparing them for stimulation. Cannon[16, 17] and Carlson[15] have reported significant results from cutting the extrinsic nerves to the stomach. We were unable to record any constant or permanent changes in motility or tonus of the sphincter or antrum or first part of the duodenum. However, the experiments of Carlson as well as those of Cannon extended over a long period of time while our methods were adapted to record only rather abrupt changes in tonus or changes in the rhythm or force of the contractions. These did not occur under our observation and we can say with certainty that section of one or all of the nerves (vagi and splanchnics) to this region does not abolish the rhythm or seriously interfere with the tonus during the time of a single experiment under anesthesia.

2. *The Effect of Vagus Stimulation.*—Stimulation of the vagi usually produces an increase in the tonus of the pyloric sphincter. The latent period is brief, generally not longer than 5 seconds. The increase in tonus is abrupt and reaches its maximum with the first or (rarely) the second contraction; it then gradually returns to normal or below, whether or not the stimulus is continued. We have not observed a continual increase in the tonus of the sphincter with each succeeding stimulation as reported by Langley[11] and others (Figs. 2 and 3).

Primary decrease in tonus was observed to follow vagus stimulation with a weak current in two animals (Fig. 4). In both cases the sphincter only was under observation. Weak currents were tried in many other experiments but in these threshold currents produced primary increase in tonus. In both the experiments in which inhibition was observed it was replaced by motor effects when the strength of the current was increased. In one instance gradually

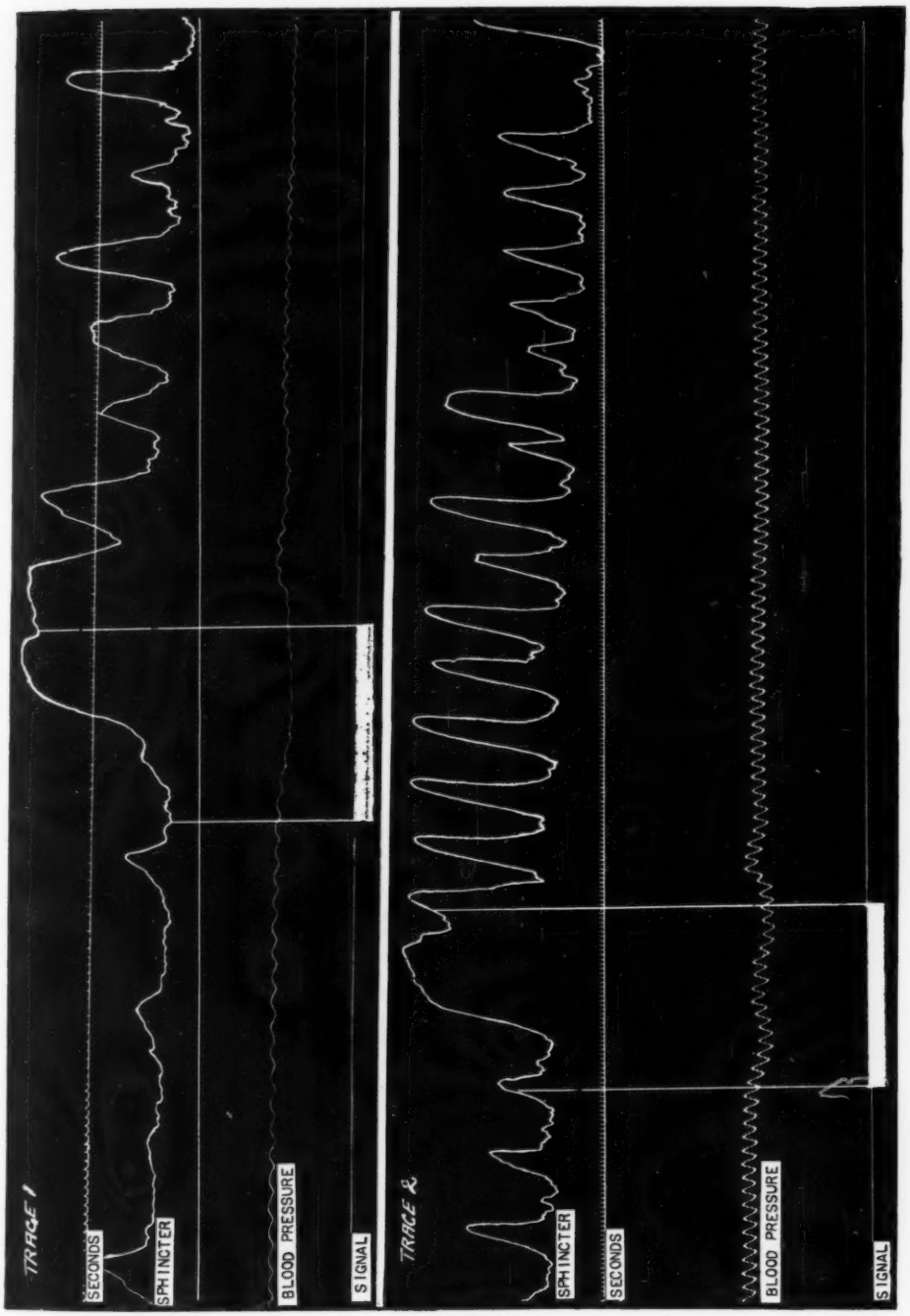


Fig. 3.—Two graphs showing the effect of vagus stimulation below the heart on the rhythm and tonus of the pyloric sphincter; trace 1, experiment 20, January 24, 1920. Ether used throughout experiment; trace 2, experiment 42, May 3, 1920, ether used throughout experiment. Secondary of Du Bois Raymond coil at 5 cm. in both cases.

Note the slight fall of blood pressure in each case, also the fact that motor responses may be obtained in a condition of great circulatory weakness. Note also the increase in the frequency of rhythmic contractions in both cases, more marked in trace 1 where the rhythm had become abnormally slow. The effect on rhythm persists after the stimulus has ceased.

increasing the strength of the stimulus diminished the inhibitory effect after it had reached a maximum. With a medium current no effect was produced. A further increase produced a motor effect which increased in extent as still stronger currents were applied.

It has recently been shown that the pyloric sphincter executes rhythmic contractions[5] and that these bear a definite relationship to the rhythmic activity of the pyloric antrum.[6] These have been observed to continue with undiminished force and normal rhythm after section of both vagi and both splanchnics, however, they are characteristically influenced by stimulation of these nerves.

During vagus stimulation the force of the rhythmic contractions increases

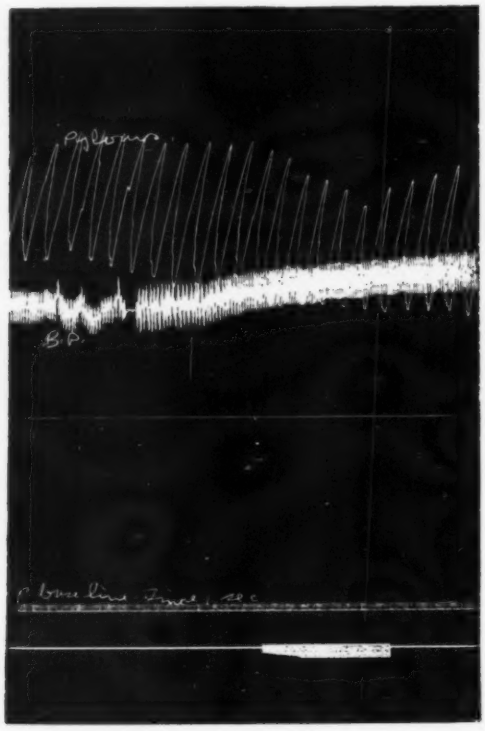

Fig. 4.—Tracing showing decrease in tonicity of the pyloric sphincter as a result of vagus stimulation. Obtained from experiment 37, March 23, 1920; secondary coil at 8 cm.; ether for operation, records obtained under morphine, 10 mm. per kg. of dog.

in nearly every case, but because of the increase in tonus and consequent lessened relaxation, the total excursion may be lessened at first. Frequently there is a spasm of the muscle which abolishes the rhythm entirely for a few seconds. At least such would be inferred from the appearance of the records. It may be well to bear in mind the limitations of the apparatus and what appears to be a spasm abolishing rhythm may very well be merely a contraction of sufficient force to obliterate the lumen of the balloon. Contraction occurring beyond this point would fail to be recorded. However, perfectly flat plateau traces such as would appear under these conditions are rare among our records.

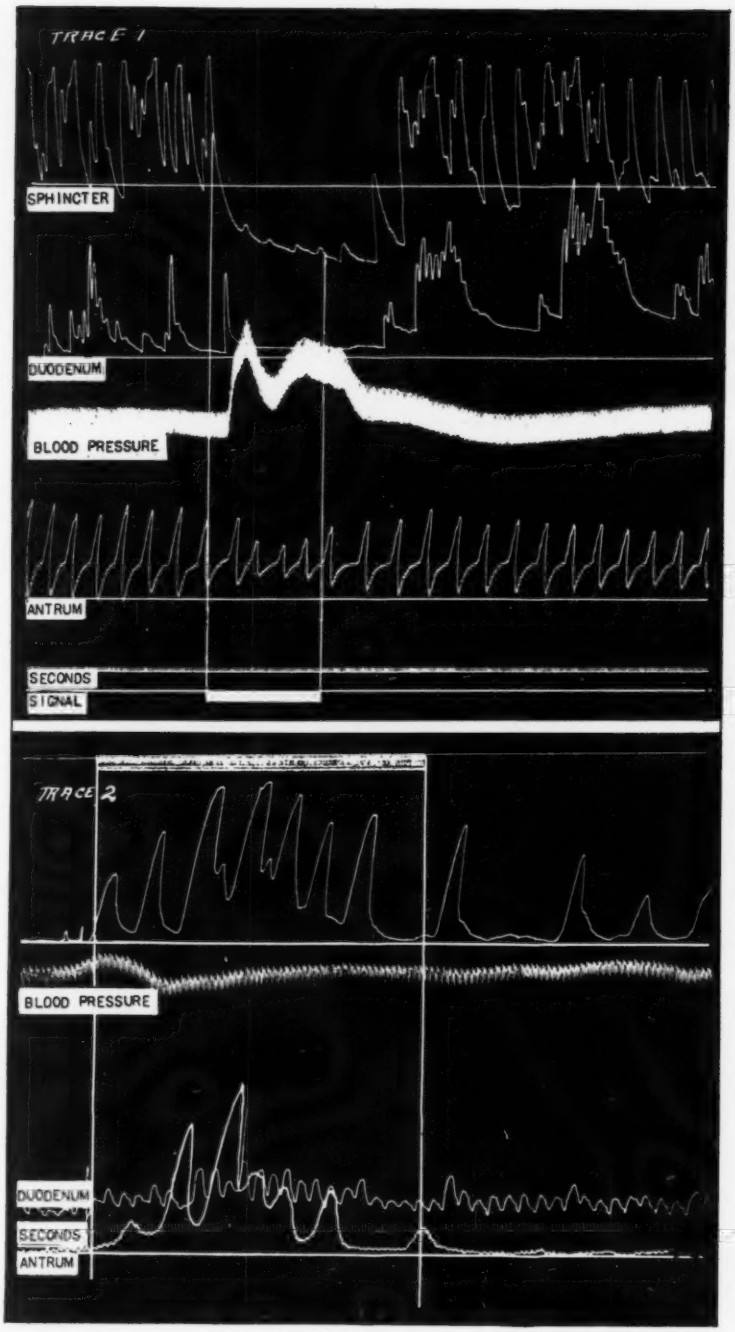


Fig. 5.—Tracings showing the effect of stimulation of the distal stump of the cut splanchnic nerve. on the motility of the pyloric sphincter, antrum, and duodenum, and the blood pressure. Trace 1, experiment 22, February 1, 1920; ether used throughout experiment; left splanchnic nerve stimulated; secondary at 8 cm. Trace 2, experiment 26, February 14, 1920; ether for operation, sodium veronal following operation. Left splanchnic stimulated, secondary at 14 cm. (Du Bois Raymond Coil.)

Note similarity of responses of sphincter, antrum, and duodenum in both cases; also that inhibition appears associated with marked vascular change, and that contraction is associated with a slight vascular effect.

On the rhythm or frequency of the contractions, stimulation of the vagi produces variable effects. A definite increase in the rate is a frequent result, especially when the rhythm has become very much slowed (Fig. 3). If the contractions have ceased they will return for a short time under effective vagus stimulation. The frequency of normal vigorous contractions remains for the most part unaltered or is only slightly increased. Slowing of the rate is not uncommon as an after effect of the stimulation; one or two contractions may be missed because of excessive tonus, or in rare cases, during a period of relaxation.

3. *The Effect of Stimulation of the Splanchnic Nerves.*—Stimulation of the splanchnics produces effects that differ a great deal, not so much in different dogs but in the same dog at different times in the experiment. We were unable to find among the factors within our control the conditions responsible for the variations. Three more or less distinct effects were recognized:

(1) Pure motor, resulting in an increase in tonus, and an increase in the strength of the rhythmic contractions of the antrum and sphincter, and frequently also of the first part of the duodenum. These effects differ only slightly from typical vagus motor effects; the chief difference is that the effect on tonus develops less abruptly, the maximum effect appearing with the third or fourth contraction instead of the first or second. Also the increase in the force of the contractions is usually less marked than after stimulation of the vagus (Fig. 5, Trace 2).

(2) Pure inhibitory, characterized by a marked loss of tonus and a complete cessation of the rhythmic contractions or a decided decrease in their force (Fig. 5, Trace 1).

(3) Mixed effects of various sorts. In many cases there was an increase in the tonus with a decrease in the force of the contractions (Fig. 6, Traces 1 and 3). Frequently the force of the contractions diminished without any apparent effect on tone. In many cases there was a primary motor effect followed by inhibition, and in others a primary inhibitory effect followed by an increase in the tonus or in the force of the contractions.

A matter of special interest in this connection is the relation of inhibitory and excitatory responses in the pars pylorica to vascular changes. As we recorded the blood pressure in practically all of our experiments we had an opportunity to observe this relationship. Our results show that in a majority of instances, motor responses in the pars pylorica from splanchnic stimulation were associated with changes in the blood pressure which were slight or in a contrary direction, that is, there was a fall instead of a rise in the blood pressure. On the other hand, in nearly every case inhibition was associated with a striking increase in the blood pressure. But the case is not quite as simple as these statements would indicate, for in certain instances (Fig. 6) a marked rise in the blood pressure is seen associated with motor responses in the gastric musculature, at least as regards tonus.

One type of mixed response which is very common and which perhaps has unusual significance in this connection develops as follows: After the usual latent period, and associated with the primary rise in the blood pressure, there

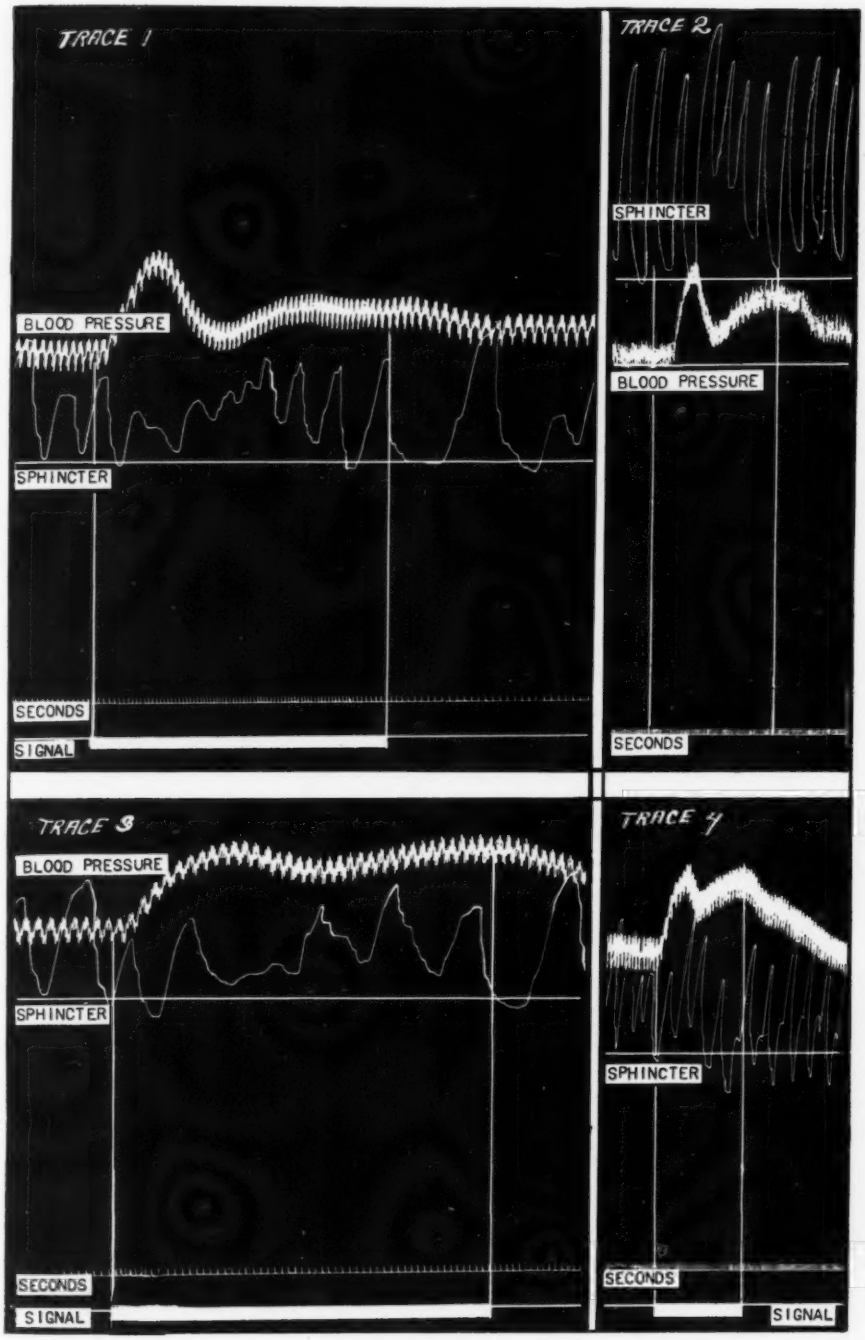


Fig. 6.—Tracings showing typical sphincter responses to splanchnic stimulation and the relation between the tonus of the sphincter and the blood pressure level during stimulation. Trace 1, experiment 19, January 22, 1920; ether used throughout experiment; right splanchnic stimulated; secondary coil at 1 cm. Trace 2, same experiment and conditions as for trace 1. Trace 3, experiment 20, January 24, 1920; left splanchnic stimulated; secondary coil at 14 cm. (Du Bois Raymond Coil.) Ether used throughout experiment. Trace 4, same as trace 3; secondary coil at 6 cm.

Note the reciprocal relation between the blood pressure level and the tonus of the sphincter.

is a slight decrease in the height of one or two contractions, but not enough to class as definite inhibition; then as the blood pressure falls, as it usually does after the primary rise, the tonus increases and the contraction which coincides with the lowest point in the blood pressure traces a curve which is higher than any other during the stimulation and frequently higher than the previous normal. As the secondary rise in the blood pressure appears the tonus falls and the strength of the individual contraction diminishes. In many cases the stimulation is followed by an increase in the tonus and the force of the contractions. These changes are shown in their most typical form in Figure 6, Trace 4, but the reciprocal relation between the tonus of the sphincter and the height of the blood pressure is apparent in all of the tracings of this figure. In Figure 5, the relation of pure motor and inhibitory reactions to the extent of the blood pressure changes is shown.

In contrast with the striking relationship seen to exist between the blood pressure changes and motor and inhibitory responses of the pylorus when these are produced by splanchnic stimulation is the absolute lack of a similar relationship when the changes are produced by vagus stimulation. As pointed out before, the motor effects following vagus stimulation are not in the least prevented by the circulatory embarrassment which accompanies stimulation of this nerve above the heart, especially in the dog. This fact is brought out in Figure 2. In Trace 2 the vagus was stimulated in the neck and the sharp drop in the blood pressure is shown. In Trace 1 the nerve was stimulated below the heart but the results are practically identical with those of Trace 2.

4. *Results Obtained when Recording Antrum, Sphincter, and Duodenum Simultaneously.*—In every instance in which simultaneous records have been obtained showing the effect of stimulating the extrinsic nerves to the antrum, sphincter, and first part of the duodenum, all of these structures have responded in the same way. Figure 2 shows two vagus motor responses affecting all three structures. Figure 5, Trace 1, shows splanchnic inhibition affecting all three simultaneously, while Trace 2 of this figure shows a splanchnic motor effect on all three at the same time. In the two instances in which we obtained inhibition over the vagus the sphincter alone was under observation so we are unable to say if the antrum and duodenum were affected in like manner.

## SUMMARY OF EXPERIMENTAL RESULTS

In tabulating our results little attention has been given to the individual animal. The reason for this is that all the animals gave fairly uniform responses (with two exceptions) to vagus stimulation and the variations encountered on splanchnic stimulation were more often met with in the same animal at different times in the experiment than in different animals. No special variations in the technic were attempted for the purpose of varying the response and the quantitative data presented may be assumed to represent the results that may be expected from nerve stimulation with the ordinary "tetanizing" induced current in routine experiments. Table I refers to the sphincter only.

TABLE I

SHOWING THE EFFECTS OF ELECTRICAL STIMULATION OF THE EXTRINSIC NERVES OF THE PYLORIC SPHINCTER

| | NO. | PER CENT | MASS ACTION PER CENT |
|---|---|---|---|
| *A. Vagus Stimulation* | | | |
| 1. Pure motor response | 53 | 64.64 | = 89.03 |
| 2. Primary motor, seconday inhibition | 20 | 24.39 | |
| 3. Pure inhibition (2 animals) | 5 | 6.09 | = 10.96 |
| 4. Primary inhibition, secondary motor | 4 | 4.87 | |
| Total | 82 | 100.00 | 100.00 |
| *B. Splanchnic Stimulation* | | | |
| 1. Pure Motor | 29 | 32.58 | = 62.91 |
| 2. Mixed, mainly motor | 27 | 30.33 | |
| 3. Pure inhibition | 28 | 31.48 | = 37.09 |
| 4. Mixed, Mainly inhibition | 5 | 5.61 | |
| Total | 89 | 100.00 | 100.00 |

As shown in Table I, of 82 vagus stimulations, 53, or 65 per cent, gave pure motor results; 20, or 24 per cent, gave primary motor and secondary inhibitory results; 5, or 6 per cent, gave pure inhibition, and 4, or 5 per cent, gave primary inhibition and secondary motor results.

Of 89 splanchnic stimulations 29, or 33 per cent, gave pure motor results; 27, or 30 per cent, gave mixed results which were mainly motor; 28, or 32 per cent, gave pure inhibition, and 5, or 5.6 per cent, were mixed results in which inhibition predominated.

Classifying all responses as motor or inhibitory according to which type of result predominated we have for vagus stimulation 89 per cent motor and 11 per cent inhibitory responses, a ratio of 8 motor to 1 inhibitory response. Splanchnic stimulation gave 63 per cent motor and 37 per cent inhibitory results, a ratio of 5 motor to 3 inhibitory. Of all stimulations, vagus and splanchnic, the responses were 76 per cent motor and 24 per cent inhibitory, a ratio of 3 motor to one inhibitory response. From these figures it will be seen that motor responses predominate among the results of splanchnic stimulation.

## DISCUSSION

While this investigation was undertaken primarily to obtain more information concerning the nervous control of the pyloric sphincter, it afforded an opportunity to observe the reactions of the antrum and first part of the duodenum to stimulation of the extrinsic nerves and to compare these with the reactions of the sphincter. The fact that in every instance in which the reactions were compared they were found to be similar, may, while not conclusive alone, serve as additional evidence for assuming the functional unity of these parts. It seems at least to be opposed to the theory of Gaskell that the pyloric sphincter is a separate structure having different nervous relations from the rest of the stomach. Further, this fact makes it possible to apply the large amount of work which has been done on the nervous control of the pyloric end of the stomach to the problem of the nervous control of the pyloric sphincter and to apply the results described for the sphincter to the stomach as a whole, at least to the pyloric portion. Such an application is further justified by the

fact that our results on the sphincter are in accord with the findings of a majority of the workers who have studied the adjacent portions of the stomach. In fact the demonstration of motor and inhibitory fibers in both the vagi and splanchnics by a single method eliminates many apparent discrepancies in previous work.

One fact which seems worthy of particular emphasis is that splanchnic motor effects are distinctly not exceptional but occur with greater frequency than inhibitory results. On the other hand, while in our experiments vagus inhibitory responses are rare, they are by no means so when appropriate methods are used for their demonstration. There is a tendency to lose sight of this fact in considering the nervous physiology of the stomach. It is not uncommon in recent clinical literature as well as in text books of physiology to find the vagus referred to as the motor nerve to the stomach and the splanchnics as inhibitors. This is doubtless due to the influence of the current classification of the autonomic nerves as sympathetic and parasympathetic, a division which has never been shown to apply to the stomach. It seems entirely possible that further study will limit its application to other structures. In this connection the following personal communication from Kuntz[34] is of interest:

"In embryos of types of all classes of vertebrates, including man, cells of medullary and neural crest origin advance peripherally along the fibers of the motor and sensory roots respectively of the spinal nerves. Some of these cells advance into the primordia of the sympathetic trunks and prevertebral plexuses and give rise to sympathetic neurones. The neurones in the cranial sympathetic ganglia arise from cells which advance peripherally along the cranial nerves with which these ganglia are genetically associated. Likewise the neurones in the pulmonary, cardiac and enteric plexuses are derived primarily from cells which advance peripherally along the fibers of the vagus. Inasmuch as the cells which advance peripherally along the spinal and cranial nerves respectively are homologous in origin, and there are no other known sources of sympathetic neurones, embryologic studies afford no basis for functional classification of parts of the sympathetic nervous system."

An interesting comparison is possible of the nervous control of the three sphincters of the alimentary canal. It is now pretty definitely established that the cardiac sphincter is controlled entirely by the vagus.[11] The results here presented as well as the literature cited show quite conclusively that the pyloric sphincter has a double nerve supply part of which is of bulbar origin, coursing over the vagi and part of spinal origin distributed through the splanchnics. The origin and course of these nerves apparently does not determine their function. The ileocolic sphincter appears[35] to receive its nerve supply entirely from nerves of spinal origin. There is in this arrangement much more of a suggestion of anatomic convenience than there is of a special innervation of the sphincters based on their development as suggested by Gaskell, or of a specialization of function by autonomic nerves based on the anatomic course of the fibers.[36]

Throughout this discussion we have assumed that the results obtained by the electrical stimulation of nerve trunks represent the functions which are

normally mediated through these nerves when excited in a reflex manner. There seems to be no reason to doubt this assumption when changes in motility are the only effects to be observed, for example, when the vagus is stimulated below the heart. However, when motor phenomena are associated with marked changes in the circulation the question may properly be raised as to how much of the observed changes in motility is due to nerve fibers having a specific function and how much to vascular changes. May,[21] from his studies, reaches the conclusion that any effect produced by stimulation of the splanchnics, generally consisting in a diminution of motor activity, is probably due to the simultaneous effect on the vascular supply to the organ. A constriction of the blood vessels, in his estimation, produces an artificial anemia which in itself is sufficient to account for diminished gastric motor activity.

Superficially the results obtained on splanchnic stimulation appear to confirm the contention of May to some extent. In nearly every case a marked rise in the blood pressure was associated with inhibitory responses in the gastric musculature and when motor effects were obtained the vascular reaction was slight. While this is the rule there are some striking exceptions, Figure 6, Trace 2, for example. These are sufficiently frequent to discount any conclusions which may be drawn from this fact alone. Before concluding that anemia is the cause of the inhibitory responses it would also be necessary to explain why motor responses are regularly obtained on stimulation of the vagus in the neck when this causes complete stoppage of the heart for some seconds (Fig. 2, Trace 2). Certainly the failure of the circulation produced in this manner must be as complete as any caused by local vasoconstriction and yet the gastric muscle shows the same motor response as when the stimulation is accomplished without interfering with the circulation.

Obviously there is some other factor concerned in the more or less constant association of marked vascular changes and gastric inhibition when these are produced by splanchnic stimulation. In the 4 tracings shown in Figure 6 there is evident a sort of reciprocal relation between the tonus of the sphincter and the blood pressure level, but the greatest decrease in tonus does not appear until the secondary rise in the blood pressure. The secondary rise has been shown to disappear when the adrenals are ligated,[38, 39, 40] and is due to the liberation of adrenalin. It seems possible, therefore, that adrenalin may have something to do with the inhibitory responses obtained from splanchnic stimulation. This is, of course, not in keeping with the finding of Elliott[24] that the pylorus of the rabbit is contracted by adrenalin or that of Contejean[26] that adrenalin produces tetanic cramps in the toad's stomach. We were working with dogs, however, and it is entirely possible that there is a difference in the response of these animals to adrenalin. We have not made a thorough investigation of the effect of adrenalin on the dog's pylorus but from the few doses which we have given ranging from 0.2 to 0.5 mg. (total dose) we have seen only pronounced inhibition. If further investigation should confirm this result it would constitute at least one instance in which the effect of adrenalin is not identical with the effects of sympathetic stimulation.

## SUMMARY AND CONCLUSIONS

1. From a review of the literature and confirmatory experimental results it is shown that the influence of the extrinsic nerves on the motility of the pyloric sphincter is the same as their influence on the antrum. It is suggested that this fact is more in keeping with the view that regards these structures as a functional unit than with the idea that the pyloric sphincter is a separate functional entity having a special nerve supply and controlled by a special reflex mechanism.

2. Experimental evidence is produced showing that *the pyloric sphincter receives a double nerve supply consisting of motor and inhibitory nerves coursing by way of the vagi and splanchnics, both nerves being mainly motor in function. Inhibitory fibers are to be found in both nerves but more in the splanchnics than the vagi.* The innervation of the sphincters is compared and found to correspond to the segmental level from which the associated structures are supplied. Attention is called to the fact that the division of the autonomic nervous system into sympathetics and parasympathetics does not apply en masse to the stomach and pyloric sphincter.

3. A more or less constant relationship is shown to exist between changes in the blood pressure and changes in the motility of the pyloric sphincter when these are produced by splanchnic stimulation but not when produced by stimulation of the vagi. As a tentative explanation for this phenomenon it is suggested that the action of the inhibitory fibers in the splanchnics may be augmented by the liberation of adrenalin. Vascular changes alone are not considered sufficient to account for the results obtained.

## REFERENCES

[1]Cannon, W. B.: The Mechanical Factors of Digestion, New York, 1911, Longmans, Green & Co. 227 pages.

[2]Gaskell, W. H.: The Involuntary System, London, 1916, Longmans, Green & Co. 178 pages.

[3]Cole, L. G.: Physiology of the Pylorus, Pilleus Ventriculi and Duodenum as Observed Roentgenographically, Jour. Am. Med. Assn., 1913, lxi, 762-766; Amer. Jour. Physiol., 1916-17, xlii, 618-619.

[4]Luckhardt, A. B., Phillips, H. T., and Carlson, A. J.: Contribution to the Physiology of the Stomach. The Control of the Pylorus, Amer. Jour. Physiol., 1919-20, i, 57-66.

[5]Wheelon, Homer, and Thomas, J. E.: Rhythmicity of the Pyloric Sphincter, Amer. Jour. Physiol., 1921, liv, 460-473.

[6]Wheelon, Homer, and Thomas, J. E.: Observations on the Motility of the Antrum and the Relation of Rhythmic Activity of the Pyloric Sphincter to that of the Antrum, Jour. Lab. and Clin. Med., 1920, vi, 124-143.

[7]McClure, C. W., Reynolds, L., and Schwartz, C. O.: On the Behavior of the Pyloric Sphincter in Normal Man, Arch. Int. Med., 1920, xxvi, 410-423.

[8]Openchowski, Th.: Ueber die nervösen Vorrichtungen des Magens Experimentelle Studien, Zentralbl. f. Physiol., 1889, iii, 1-10; Arch. f. Anat. u. Physiol., 1889, p. 549.

[9]Katz and Winkler: Beitr. Exp. Path. aus Lab. von Basch, 1902, Quoted from Elliott[35].

[10]Dixon, W. E.: The Innervation of the Frog's Stomach, Jour. Physiol., 1902, xxviii, 57-75.

[11]Langley, J. N.: On Inhibitory Fibres in the Vagus for the end of the Esophagus and the Stomach, Jour. Physiol., 1898-99, xxiii, 407-414.

[12]Morat, J. P.: Sur Quelques particularités de l'innervation motrice de l'estomac et de l'intestin, Arch. de Physiol., Paris, S. 5., 1893, v, 142-153.

[13]Morat, J. P.: Sur l'innervation motrice de l'estomac, Lyon Méd., 1882, xl, 289-335.

[14]Patterson, T. L.: Vagus and Splanchnic Influence on the Gastric Hunger Movements of the Frog, Amer. Jour. Physiol., 1920, liii, 293.

[15]Carlson, A. J.: Contributions to the Physiology of the Stomach. The Inhibitory Reflexes from the Gastric Mucosa, Amer. Jour. Physiol., 1913, xxxii, 388-397. A Study of the

Mechanism of the Hunger Contractions of the Empty Stomach by Experiments on Dogs, ibid, 369-388.

[16]Cannon, W. B.: The Motor Activities of the Stomach and Small Intestine after Splanchnic and Vagus Section, Am. Jour. Physiol., 1906-1907, xvii, 429-442.

[17]Cannon, W. B.: The Nature of Gastric Peristalsis, Am. Jour. Physiol., 1911, xxix, 250.

[18]Pavlov, I. P.: The Work of the Digestive Glands, Trs. W. H. Thompson, Ed. 2, London, 1910, Chas. Griffin & Co., 266 pages.

[19]Kelling, G.: Untersuchungen über die Spannungszustände der Bauchwand, der Magen und der Darmwand, Ztschr. f. Biol., 1903, xliv, 161-258.

[20]Duceschi, V.: Sui nervi della stomaco contributo alla conoscenza della innervazione viscerale, Arch. di. Fisiol., Firenze, 1905, ii, 521-548.

[21]May, W. P.: The Innervation of the Sphincters and Musculature of the Stomach, Jour. Physiol., 1904, xxxi, 262-271; 1901, xxvii, 250.

[22]Wertheimer, E.: Inhibition Réflex du tonus et des mouvements de l'estomac, Arch. de Physiol. norm. et path., Paris, 5 s., 1891, iv, 379-385.

[23]Auer, J.: The Effect of Severing the Vagi or the Splanchnics or Both upon Gastric Motility in Rabbits, Amer. Jour. Physiol., 1909-10, xxv, 334-344.

[24]Elliott, T. R.: The Action of Adrenalin, Jour. Physiol., 1905, xxxii, 401-467.

[25]Schiff: Moleschott's Untersuchungen, 1862, viii, 527.

[26]Contejean, Ch.: Action des nerfs pneumogastrique et grand sympathetique, Arch. de Physiol. norm. et path., Paris, 1892, iv, 640-650.

[27]Courtade, D., and Guyon, J. F.: Excitabilité comparié du pneumogastrique et du sympathetique thoraciques, Compt. rend. Soc. de biol., 1900, lii, 532-534.

[28]Waters, W. H.: Some Vasomotor Functions of the Spinal Nerves in the Frog, Jour., Physiol., 1885, vi, 460-463.

[29]Steinach, E., and Wiener, H.: Moyorische Functionen hinterer Spinalnervenwurzeln, Arch. f. d. ges. Physiol., 1895, lx, 593-622.

[30]Oser, L.: Experimentelle Beiträge zur Innervation des Magens, Ztschr. f. klin. Med., 1892, xx, 291-297.

[31]Bayliss, B. M., and Starling, E. H.: The Movements and Innervation of the Small Intestine, Jour. Physiol., 1899, xxiv, 99-143.

[32]Howell: Text-book of Physiology, 1918, ed. 7, W. B. Saunders Co., 1059 pages.

[33]Wheelon, Homer., and Thomas, J. E.: Observations on the Motility of the Duodenum and the Relation of Duodenal Activity to that of the Pars Pylorica, Am. Jour. Physiol., 1922, lix, 72-96.

[34]Kuntz, A.: Personal Communication to Homer Wheelon.

[35]Elliott, T. R.: On the Innervation of the Ileocolic Sphincter, Jour. Physiol., 1904, xxxi, 157-168.

[36]Langley, J. N.: Schäfer's Text-book of Physiology, vol. ii. The Sympathetic and Other Allied Systems of Nerves, 1900; Das sympathische und verwandte nervöse Systeme der Wirbeltiere (Anatonoms nervöse System). Ergebn. Physiol., 1903, ii, 830-872.

[37]Gaskell, W. H.: On the Structure, Distribution and Function of Nerves Which Innervate Visceral and Vascular Systems, Jour. Physiol., 1886, vii, 1-80.

[38]Elliott, T. R.: The Control of the Suprarenal Glands by the Splanchnic Nerves, Jour. Physiol., 1912, xliv, 374-409.

[39]von Anrep, G.: On Local Vascular Reactions and their Interpretation, Jour. Physiol., 1912, xlv, 318-327. On the Part Played by the Suprarenals in the Normal Vascular Reactions of the Body, Jour. Physiol., 1912, pp. 307-317.

[40]Pearlmann, I., and Swale, Vincent: The Function of the Chromaphil Tissue, Endocrinology, 1919, iii, 121-136.

# BLOOD PRESSURE STUDIES IN ONE HUNDRED AND FORTY CASES OF DIABETES MELLITUS*

By Jacob Rosenbloom, M.D., Ph.D., Pittsburgh

## I

### REVIEW OF THE LITERATURE

THERE has been some difference of opinion as regards the blood pressure in diabetes mellitus. Potain[1] found the blood pressure very high, higher even than that seen in nephritis. This view is shared by Teissier,[2] while conflicting views are those of Vaquez,[3] Hensen[4] and Orr[5] who all report cases showing hypotension. Goodman[6] has seen both high and low pressures, but low pressures more frequently. Elliott[7] has reported blood pressure studies in twenty-five cases of diabetes. There were thirteen males and twelve females in this series. Their average age was forty-five, average weight one hundred and fifty-six pounds and the average systolic pressure was 127. Of the thirteen cases under fifty the average systolic pressure was 107 and the twelve cases over fifty, the average systolic pressure was 150. He thought that the low systolic pressure was due to emaciation and brown atrophy or fatty heart.

Joslin[8] presents the following table showing that the systolic pressure in diabetes is practically normal.

Table I (From Joslin).

| AGES | NO. OF CASES | AVERAGE BLOOD PRESSURE IN DIABETICS |
|---|---|---|
| 15-20 | 38 | 121 |
| 21-25 | 33 | 122 |
| 26-30 | 56 | 121 |
| 31-35 | 39 | 120 |
| 36-40 | 64 | 125 |
| 41-45 | 75 | 139 |
| 46-50 | 116 | 143 |
| 51-55 | 127 | 154 |
| 56-60 | 103 | 154 |
| Over 60 | 163 | 156 |
| Total No. of cases | 814 | Average 139 |

Kahn[9] has recently pointed out that the blood pressure is normal or slightly subnormal in diabetes. Crummer[10] found a high blood pressure in diabetes. Severie[11] reported blood pressure findings in twenty-nine cases of diabetes. He found many ranges of blood pressure up to 240. Janeway[12] states that he has seen both high and low blood pressures in diabetes, the latter in severe cases with marked emaciation and diacetic acid in the urine, the former especially in the milder forms in stout elderly people, where

*Received for publication, July 20, 1921.

TABLE II

| CASE NO. | AGE | SEX | AGE AT ONSET OF THE DISEASE | BLOOD PRESSURE SYS. | DIAST. | PULSE PRES. | REMARKS |
|---|---|---|---|---|---|---|---|
| 1 | 20 | F | 19 | 120 | 80 | 40 | Sugar in urine |
| 1 | 21 | | | 120 | 80 | 40 | Sugar in urine |
| 2 | 44 | F | 44 | 140 | 90 | 50 | Sugar in urine |
| 2 | 45 | | | 140 | 90 | 50 | Sugar free |
| 2 | 46 | | | 140 | 90 | 50 | Sugar free |
| 3 | 55 | F | 44 | 130 | 90 | 40 | Sugar in urine |
| 3 | 56 | | | 130 | 85 | 45 | Sugar free |
| 4 | 26 | F | 23 | 100 | 60 | 40 | (Died in coma, six hours later) |
| 5 | 54 | F | 54 | 140 | 100 | 40 | Sugar in urine |
| 5 | 55 | | | 140 | 95 | 45 | Sugar free |
| 6 | 54 | M | 54 | 170 | 100 | 70 | Patient has nephritis |
| 7 | 54 | F | 51 | 210 | 110 | 100 | Sugar in urine |
| 7 | 55 | | | 200 | 110 | 90 | Sugar in urine |
| 8 | 29 | F | 29 | 130 | 80 | 50 | Sugar in urine |
| 8 | 30 | | | 125 | 80 | 45 | Sugar free |
| 9 | 59 | M | 58 | 145 | 90 | 55 | Sugar in urine |
| 9 | 60 | | | 145 | 90 | 55 | Sugar free |
| 10 | 30 | F | 30 | 130 | 90 | 40 | Sugar in urine |
| 10 | 31 | | | 130 | 90 | 40 | Sugar free |
| 11 | 37 | M | 37 | 120 | 80 | 40 | Sugar in urine |
| 11 | 38 | | | 120 | 80 | 40 | Sugar free |
| 12 | 58 | F | 50 | 120 | 60 | 60 | Sugar in urine |
| 12 | 60 | | | 130 | 70 | 60 | Sugar free |
| 12 | 62 | | | 130 | 70 | 60 | Sugar free |
| 12 | 63 | F | | 135 | 75 | 65 | Sugar free |
| 12 | 64 | | | 140 | 80 | 60 | Sugar free |
| 13 | 48 | M | 48 | 140 | 90 | 50 | Sugar in urine |
| 13 | 49 | | | 140 | 90 | 50 | Sugar free |
| 14 | 60 | F | 60 | 210 | 140 | 70 | Patient has nephritis |
| 14 | 61 | | | 200 | 140 | 60 | Sugar in urine |
| 15 | 19 | M | 19 | 120 | 70 | 50 | Sugar in urine |
| 15 | 20 | | | 120 | 80 | 40 | Sugar free |
| 16 | 53 | F | 50 | 150 | 100 | 50 | Sugar in urine |
| 16 | 54 | | | 150 | 100 | 50 | Sugar free |
| 16 | 55 | | | 145 | 95 | 50 | Sugar free |
| 16 | 56 | | | 150 | 100 | 50 | Sugar free |
| 16 | 57 | | | 155 | 100 | 50 | Sugar free |
| 16 | 58 | | | 170 | 100 | 70 | Sugar free |
| 17 | 53 | F | 60 | 150 | 90 | 60 | Sugar in urine |
| 17 | 54 | | | 150 | 90 | 60 | Sugar free |
| 17 | 56 | | | 155 | 95 | 60 | Sugar free |
| 18 | 55 | M | 50 | 150 | 90 | 60 | Died in coma next day |
| 19 | 35 | M | 35 | 130 | 90 | 40 | Sugar in urine |
| 19 | 35 | | | 130 | 90 | 40 | Sugar free |
| 20 | 49 | M | 49 | 150 | 90 | 60 | Sugar in urine |
| 20 | 50 | | | 150 | 90 | 60 | Sugar free |
| 21 | 69 | M | 65 | 170 | 90 | 80 | Sugar in urine |
| 21 | 70 | | | 170 | 90 | 80 | Sugar free |
| 21 | 71 | | | 170 | 90 | 80 | Sugar free |
| 22 | 65 | M | 35 | 210 | 100 | 110 | Sugar in urine |
| 22 | 66 | | | 200 | 100 | 100 | Sugar free Has nephritis |
| 22 | 67 | | | 200 | 100 | 100 | Sugar free |
| 23 | 11 | F | 11 | 90 | 50 | 40 | Sugar in urine |
| 23 | 12 | | | 90 | 50 | 40 | Sugar free |
| 24 | 8 | M | 7 | 80 | 45 | 35 | Sugar in urine |
| 24 | 9 | | | 80 | 45 | 35 | Sugar free |
| 25 | 42 | M | 40 | 120 | 70 | 50 | Sugar in urine |
| 25 | 43 | | | 120 | 70 | 50 | Sugar free |
| 25 | 44 | | | 120 | 70 | 50 | Sugar free |
| 26 | 51 | M | 48 | 140 | 90 | 50 | Sugar in urine |
| 26 | 53 | | | 145 | 95 | 50 | Sugar free |

TABLE II—CONT'D.

| CASE NO. | AGE | SEX | AGE AT ONSET OF THE DISEASE | BLOOD PRESSURE SYS. | DIAST. | PULSE PRES. | REMARKS |
|---|---|---|---|---|---|---|---|
| 27 | 52 | M | 52 | 140 | 90 | 50 | Sugar in urine |
| 27 | 54 | | | 140 | 90 | 50 | Sugar in urine |
| 28 | 59 | M | 59 | 150 | 90 | 60 | Sugar in urine |
| 28 | 60 | | | 150 | 90 | 60 | Sugar free |
| 29 | 61 | F | 61 | 210 | 100 | 110 | Sugar in urine. Has nephritis |
| 29 | 63 | | | 210 | 100 | 110 | Sugar free |
| 30 | 12 | F | 10 | 100 | 60 | 40 | Sugar in urine |
| 30 | 13 | | | 100 | 60 | 40 | Sugar free |
| 31 | 45 | M | 40 | 140 | 100 | 40 | Sugar in urine |
| 31 | 46 | | | 140 | 100 | 40 | Sugar in urine |
| 32 | 32 | F | 32 | 120 | 70 | 50 | Sugar in urine |
| 32 | 33 | | | 120 | 70 | 50 | Sugar free |
| 33 | 62 | M | 58 | 160 | 100 | 60 | Sugar in urine. Has nephritis |
| 33 | 63 | | | 160 | 80 | 80 | Sugar free |
| 33 | 64 | | | 158 | 90 | 68 | Sugar free |
| 33 | 65 | | | 160 | 80 | 80 | Sugar free |
| 33 | 66 | | | 170 | 85 | 85 | Sugar free |
| 33 | 67 | | | 160 | 80 | 80 | Sugar free |
| 33 | 68 | | | 160 | 80 | 80 | Sugar free |
| 34 | 58 | F | 58 | 140 | 90 | 50 | Sugar in urine |
| 34 | 59 | | | 140 | 90 | 50 | Sugar free |
| 35 | 25 | F | 25 | 120 | 80 | 40 | Sugar in urine |
| 36 | 45 | F | 45 | 130 | 90 | 40 | Sugar in urine |
| 36 | 46 | | | 135 | 90 | 45 | Sugar free |
| 37 | 70 | F | 60 | 160 | 90 | 70 | Sugar in urine |
| 37 | 72 | | | 165 | 90 | 75 | Sugar free |
| 38 | 43 | M | 43 | 130 | 80 | 50 | Sugar in urine |
| 38 | 44 | | | 130 | 80 | 50 | Sugar free |
| 39 | 50 | M | 50 | 140 | 100 | 40 | Sugar in urine |
| 39 | 51 | | | 120 | 70 | 50 | Sugar free |
| 39 | 52 | | | 130 | 70 | 60 | Sugar free |
| 39 | 54 | | | 130 | 70 | 60 | Sugar free |
| 40 | 45 | M | 45 | 140 | 90 | 50 | Sugar in urine |
| 40 | 46 | | | 145 | 95 | 50 | Sugar free |
| 40 | 47 | | | 140 | 90 | 50 | Sugar free |
| 40 | 48 | | | 140 | 90 | 50 | Sugar free |
| 40 | 49 | | | 145 | 90 | 50 | Sugar free |
| 41 | 39 | F | 39 | 250 | 140 | 110 | Sugar in urine. Has nephritis |
| 41 | 40 | | | 200 | 130 | 70 | Sugar free |
| 41 | 41 | | | 200 | 120 | 80 | Sugar free |
| 42 | 54 | M | 54 | 130 | 70 | 60 | Sugar in urine |
| 42 | 55 | | | 130 | 70 | 60 | Sugar free |
| 42 | 56 | | | 135 | 75 | 60 | Sugar free |
| 43 | 41 | M | 41 | 130 | 90 | 40 | Sugar in urine |
| 44 | 42 | M | 42 | 140 | 90 | 50 | Sugar in urine |
| 44 | 44 | | | 140 | 90 | 50 | Sugar free |
| 45 | 34 | F | 34 | 140 | 90 | 50 | Sugar in urine |
| 46 | 60 | M | 50 | 150 | 90 | 60 | Sugar in urine |
| 47 | 40 | F | 40 | 130 | 90 | 40 | Sugar in urine |
| 47 | 45 | | | 140 | 90 | 50 | Sugar in urine |
| 47 | 46 | | | 145 | 90 | 55 | Sugar free |
| 48 | 46 | F | 43 | 150 | 90 | 60 | Sugar in urine |
| 48 | 47 | | | 150 | 90 | 60 | Sugar free |
| 48 | 48 | | | 140 | 85 | 55 | Sugar free |
| 48 | 49 | | | 150 | 90 | 60 | Sugar in urine |
| 48 | 50 | | | 150 | 90 | 60 | Sugar free |
| 49 | 32 | M | 32 | 130 | 90 | 40 | Sugar in urine |
| 49 | 33 | | | 130 | 90 | 40 | Sugar free |
| 49 | 34 | | | 130 | 90 | 40 | Sugar free |
| 50 | 47 | M | 44 | 150 | 80 | 70 | Sugar in urine |

TABLE II—CONT'D.

| CASE NO. | AGE | SEX | AGE AT ONSET OF THE DISEASE | BLOOD PRESSURE SYS. | DIAST. | PULSE PRES. | REMARKS |
|---|---|---|---|---|---|---|---|
| 50 | 48 | | | 150 | 80 | 70 | Sugar free |
| 51 | 58 | F | 58 | 130 | 90 | 40 | Sugar in urine |
| 51 | 59 | | | 130 | 90 | 40 | Sugar free |
| 51 | 60 | | | 130 | 90 | 40 | Sugar free |
| 52 | 48 | F | 46 | 140 | 90 | 50 | Sugar free |
| 53 | 48 | F | 47 | 140 | 80 | 60 | Sugar in urine |
| 54 | 51 | M | 50 | 95 | 80 | 15 | Sugar in urine |
| 54 | 52 | | | 120 | 80 | 40 | Sugar free. Myocard. |
| 54 | 53 | | | 95 | 80 | 15 | Died cardiac dilatation |
| 55 | 50 | F | 49 | 140 | 90 | 50 | Sugar in urine |
| 55 | 51 | | | 140 | 90 | 50 | Sugar free |
| 56 | 54 | M | 52 | 150 | 90 | 60 | Sugar in urine |
| 56 | 55 | | | 150 | 90 | 60 | Sugar free |
| 57 | 32 | M | 32 | 130 | 85 | 45 | Sugar in urine |
| 57 | 33 | | | 130 | 90 | 40 | Sugar free |
| 58 | 39 | M | 39 | 140 | 90 | 50 | Sugar in urine |
| 59 | 58 | M | 44 | 160 | 90 | 70 | Sugar in urine |
| 59 | 59 | | | 150 | 90 | 60 | Sugar free |
| 59 | 60 | | | 155 | 90 | 65 | Sugar free |
| 60 | 60 | M | 58 | 120 | 70 | 50 | Sugar in urine |
| 60 | 61 | | | 130 | 80 | 50 | Sugar free |
| 61 | 50 | F | 49 | 140 | 90 | 50 | Sugar in urine |
| 62 | 50 | F | 46 | 140 | 80 | 60 | Sugar in urine |
| 62 | 51 | | | 140 | 80 | 60 | Sugar free |
| 62 | 52 | | | 150 | 90 | 60 | Sugar free |
| 62 | 53 | | | 150 | 90 | 60 | Sugar free |
| 62 | 54 | | | 150 | 90 | 60 | Sugar free |
| 62 | 55 | | | 150 | 90 | 60 | Sugar free |
| 62 | 56 | | | 155 | 95 | 60 | Sugar free |
| 63 | 69 | M | 67 | 160 | 90 | 70 | Sugar in urine |
| 64 | 44 | M | 44 | 120 | 80 | 40 | Sugar in urine |
| 64 | 45 | | | 130 | 90 | 40 | Sugar free |
| 65 | 58 | F | 55 | 150 | 90 | 60 | Sugar in urine |
| 65 | 59 | | | 155 | 95 | 65 | Sugar free |
| 65 | 60 | | | 160 | 100 | 60 | Sugar free |
| 65 | 61 | | | 160 | 90 | 70 | Sugar free |
| 66 | 57 | M | 57 | 130 | 90 | 40 | Sugar in urine |
| 66 | 58 | | | 135 | 95 | 45 | Sugar free |
| 67 | 48 | M | 48 | 150 | 90 | 60 | Sugar in urine |
| 67 | 49 | | | 150 | 95 | 55 | Sugar free |
| 68 | 57 | M | 50 | 160 | 85 | 75 | Sugar in urine |
| 69 | 47 | M | 47 | 140 | 100 | 40 | Sugar in urine |
| 70 | 54 | M | 51 | 120 | 80 | 40 | Sugar in urine |
| 70 | 55 | | | 120 | 80 | 40 | Sugar in urine |
| 70 | 56 | | | 120 | 80 | 40 | Sugar free |
| 71 | 36 | F | 35 | 120 | 80 | 40 | Sugar in urine |
| 71 | 37 | | | 120 | 80 | 40 | Sugar free |
| 71 | 38 | | | 120 | 80 | 40 | Sugar free |
| 72 | 43 | M | 40 | 120 | 70 | 50 | Sugar in urine |
| 72 | 44 | | | 120 | 70 | 50 | Sugar free |
| 73 | 45 | M | 45 | 125 | 75 | 50 | Sugar free |
| 74 | 68 | F | 66 | 210 | 80 | 130 | Sugar in urine. Has nephritis |
| 74 | 69 | | | 200 | 80 | 120 | Sugar free |
| 75 | 40 | F | 40 | 140 | 100 | 40 | Sugar in urine |
| 75 | 40 | | | 140 | 100 | 40 | Sugar free |
| 76 | 41 | M | 39 | 130 | 90 | 40 | Sugar in urine |
| 76 | 42 | | | 130 | 90 | 40 | Sugar free |
| 76 | 43 | | | 140 | 100 | 40 | Sugar free |
| 77 | 74 | M | 67 | 150 | 100 | 50 | Sugar in urine |
| 77 | 75 | | | 160 | 100 | 60 | Sugar free |
| 78 | 55 | F | 52 | 140 | 100 | 40 | Sugar in urine |
| 79 | 52 | M | 52 | 140 | 90 | 50 | Sugar in urine |

TABLE II—CONT'D.

| CASE NO. | AGE | SEX | AGE AT ONSET OF THE DISEASE | BLOOD PRESSURE SYS. | DIAST. | PULSE PRES. | REMARKS |
|---|---|---|---|---|---|---|---|
| 79 | 52 | | | 140 | 90 | 50 | Sugar free |
| 80 | 43 | F | 40 | 130 | 80 | 50 | Sugar in urine |
| 80 | 44 | | | 130 | 80 | 50 | Sugar free |
| 81 | 58 | M | 58 | 180 | 100 | 80 | Sugar in urine. Aortitis and nephritis |
| 82 | 32 | M | 32 | 130 | 90 | 40 | Sugar in urine |
| 82 | 33 | | | 130 | 90 | 40 | Sugar free |
| 83 | 46 | M | 43 | 140 | 100 | 40 | Sugar in urine |
| 83 | 47 | | | 140 | 100 | 40 | Sugar free |
| 84 | 63 | F | 63 | 240 | 110 | 130 | Sugar in urine. Aortitis and nephritis |
| 84 | 64 | | | 220 | 110 | 110 | Sugar free |
| 85 | 46 | M | 46 | 140 | 100 | 40 | Sugar in urine |
| 85 | 46 | | | 140 | 100 | 40 | Sugar free |
| 86 | 68 | F | 68 | 200 | 110 | 90 | Sugar in urine. Patient has nephritis |
| 86 | 69 | | | 200 | 100 | 100 | Sugar free |
| 87 | 50 | F | 42 | 145 | 90 | 55 | Sugar in urine |
| 87 | 50 | | | 140 | 90 | 50 | Sugar free |
| 88 | 33 | F | 33 | 140 | 100 | 40 | Sugar in urine |
| 88 | 34 | | | 140 | 100 | 40 | Sugar free |
| 88 | 35 | | | 140 | 100 | 40 | Sugar free |
| 89 | 42 | M | 42 | 140 | 100 | 40 | Sugar free |
| 89 | 43 | | | 140 | 100 | 40 | Sugar in urine |
| 89 | 44 | | | 150 | 100 | 50 | Sugar free |
| 89 | 45 | | | 140 | 100 | 40 | Sugar free |
| 89 | 46 | | | 140 | 100 | 40 | Sugar free |
| 90 | 62 | M | 56 | 210 | 120 | 90 | Sugar in urine. Patient has nephritis |
| 90 | 62 | | | 210 | 120 | 90 | Sugar free |
| 91 | 40 | M | 40 | 150 | 100 | 50 | Sugar in urine |
| 91 | 41 | | | 140 | 100 | 40 | Sugar free |
| 91 | 42 | | | 140 | 100 | 40 | Sugar free |
| 92 | 55 | F | 52 | 210 | 100 | 110 | Sugar in urine. Patient has nephritis |
| 92 | 56 | | | 190 | 100 | 90 | Sugar free |
| 93 | 50 | M | 50 | 140 | 100 | 40 | Sugar in urine |
| 94 | 57 | M | 57 | 240 | 100 | 140 | Sugar in urine. Patient has nephritis |
| 94 | 58 | | | 190 | 100 | 90 | Sugar free |
| 94 | 59 | | | 200 | 110 | 90 | Sugar free |
| 95 | 30 | F | 30 | 120 | 80 | 40 | Sugar in urine |
| 95 | 30 | | | 120 | 80 | 40 | Sugar free |
| 96 | 42 | F | 40 | 130 | 90 | 40 | Sugar in urine |
| 96 | 43 | | | 130 | 90 | 40 | Sugar free |
| 97 | 25 | M | 24 | 130 | 90 | 40 | Sugar in urine |
| 97 | 26 | | | 130 | 90 | 40 | Sugar free |
| 97 | 27 | | | 130 | 90 | 40 | Sugar free |
| 97 | 28 | | | 130 | 90 | 40 | Sugar free |
| 98 | 35 | M | 35 | 100 | 70 | 30 | Sugar in urine |
| 98 | 36 | | | 110 | 70 | 40 | Sugar free |
| 99 | 7 | M | 6 | 90 | 60 | 30 | Sugar in urine |
| 99 | 8 | | | 90 | 60 | 30 | Sugar free |
| 100 | 50 | F | 46 | 180 | 90 | 90 | Sugar in urine. Aortitis and nephritis |
| 100 | 51 | | | 180 | 90 | 90 | Sugar free |
| 101 | 55 | M | 55 | 130 | 80 | 50 | Sugar in urine |
| 101 | 55 | | | 130 | 80 | 50 | Sugar free |
| 102 | 55 | F | 51 | 150 | 100 | 50 | Sugar in urine |
| 102 | 56 | | | 150 | 100 | 50 | Sugar free |
| 102 | 57 | | | 150 | 100 | 50 | Sugar free |
| 103 | 53 | M | 52 | 120 | 80 | 40 | Sugar in urine |
| 103 | 54 | | | 130 | 90 | 40 | Sugar free |

TABLE II—CONT'D.

| CASE NO. | AGE | SEX | AGE AT ONSET OF THE DISEASE | BLOOD PRESSURE SYS. | DIAST. | PULSE PRES. | REMARKS |
|---|---|---|---|---|---|---|---|
| 104 | 45 | F | 45 | 150 | 90 | 60 | Sugar in urine |
| 104 | 46 | | | 150 | 90 | 60 | Sugar free |
| 105 | 62 | F | 62 | 180 | 80 | 100 | Sugar in urine. Nephritis |
| 105 | 63 | | | 200 | 110 | 90 | Sugar free |
| 105 | 64 | | | 220 | 110 | 110 | Sugar free |
| 106 | 53 | F | 53 | 190 | 120 | 70 | Sugar in urine |
| 106 | | | | 190 | 110 | 80 | Sugar free |
| 107 | 56 | F | 50 | 150 | 90 | 60 | Sugar in urine |
| 107 | 56 | | | 150 | 90 | 60 | Sugar free |
| 108 | 58 | F | 53 | 150 | 90 | 60 | Sugar in urine |
| 108 | 58 | | | 150 | 90 | 60 | Sugar free |
| 109 | 53 | F | 51 | 160 | 90 | 70 | Sugar in urine |
| 109 | 53 | | | 160 | 90 | 70 | Sugar free |
| 110 | 28 | M | 28 | 125 | 70 | 55 | Sugar in urine |
| 110 | 28 | | | 120 | 80 | 40 | Sugar free |
| 111 | 33 | M | 33 | 110 | 70 | 40 | Sugar in urine |
| 111 | 34 | | | 110 | 70 | 40 | Sugar free |
| 112 | 38 | M | 38 | 130 | 90 | 40 | Sugar in urine |
| 112 | 39 | | | 130 | 90 | 40 | Sugar free |
| 113 | 42 | F | 42 | 130 | 90 | 40 | Sugar in urine |
| 113 | 43 | | | 130 | 90 | 40 | Sugar free |
| 114 | 47 | F | 40 | 120 | 80 | 40 | Sugar in urine |
| 114 | 49 | | | 130 | 90 | 40 | Sugar free |
| 115 | 60 | M | 55 | 120 | 70 | 50 | Sugar in urine |
| 115 | 61 | | | 130 | 80 | 50 | Sugar free |
| 116 | 60 | F | 50 | 210 | 110 | 100 | Sugar in urine. nephritis |
| 116 | 61 | | | 220 | 110 | 110 | Sugar free |
| 117 | 50 | F | 48 | 210 | 100 | 110 | Sugar in urine. Nephritis and aortitis |
| 117 | 51 | | | 210 | 110 | 100 | Sugar free |
| 117 | 52 | | | 200 | 100 | 100 | Sugar free |
| 117 | 53 | | | 200 | 100 | 100 | Sugar free |
| 117 | 54 | | | 210 | 110 | 100 | Sugar free |
| 117 | 55 | | | 200 | 110 | 90 | Sugar free |
| 117 | 56 | | | 200 | 100 | 100 | Sugar free |
| 118 | 53 | M | 33 | 170 | 100 | 70 | Sugar in urine |
| 118 | 54 | | | 190 | 100 | 90 | Sugar free |
| 119 | 46 | M | 45 | 150 | 100 | 50 | Sugar in urine |
| 119 | 47 | | | 150 | 90 | 60 | Sugar free |
| 120 | 62 | F | 52 | 160 | 90 | 70 | Sugar in urine |
| 121 | 33 | M | 31 | 140 | 80 | 60 | Sugar in urine |
| 121 | 35 | | | 140 | 90 | 50 | Sugar free |
| 122 | 39 | M | 39 | 130 | 90 | 40 | Sugar in urine |
| 123 | 51 | F | 47 | 110 | 80 | 30 | Sugar free |
| 124 | 49 | M | 41 | 120 | 80 | 40 | Sugar in urine |
| 124 | 50 | | | 120 | 80 | 40 | Sugar free |
| 124 | 51 | | | 130 | 90 | 40 | Sugar free |
| 124 | 52 | | | 130 | 90 | 40 | Sugar free |
| 124 | 53 | | | 135 | 90 | 45 | Sugar free |
| 124 | 54 | | | 140 | 100 | 40 | Sugar free |
| 125 | 56 | F | 56 | 180 | 100 | 80 | Sugar in urine |
| 125 | 57 | | | 190 | 100 | 90 | Sugar free |
| 126 | 41 | M | 41 | 150 | 100 | 50 | Sugar in urine |
| 126 | 42 | | | 140 | 100 | 40 | Sugar free |
| 127 | 45 | M | 45 | 140 | 80 | 60 | Sugar in urine |
| 127 | 45 | | | 140 | 80 | 60 | Sugar free |
| 128 | 55 | M | 55 | 220 | 110 | 110 | Sugar in urine. Nephritis and aortitis |
| 129 | 49 | M | 41 | 160 | 100 | 60 | Sugar in urine |
| 129 | 50 | | | 150 | 100 | 50 | Sugar free |
| 129 | 51 | | | 150 | 90 | 60 | Sugar free |

TABLE II—CONT'D.

| CASE NO. | AGE | SEX | AGE AT ONSET OF THE DISEASE | BLOOD PRESSURE SYS. | DIAST. | PULSE PRES. | REMARKS |
|---|---|---|---|---|---|---|---|
| 130 | 28 | M | 28 | 130 | 90 | 40 | Sugar in urine |
| 131 | 59 | F | 59 | 150 | 90 | 60 | Sugar in urine |
| 132 | 64 | F | 58 | 150 | 90 | 60 | Sugar in urine |
| 133 | 52 | F | 52 | 150 | 80 | 70 | Sugar in urine |
| 133 | 53 | | | 160 | 80 | 80 | Sugar free |
| 133 | 54 | | | 150 | 80 | 70 | Sugar free |
| 133 | 55 | | | 160 | 80 | 80 | Sugar free |
| 133 | 56 | | | 160 | 80 | 80 | Sugar free |
| 133 | 57 | | | 150 | 90 | 60 | Sugar free |
| 134 | 52 | F | 52 | 180 | 90 | 90 | Sugar in urine. Nephritis and aortitis |
| 134 | 53 | | | 180 | 90 | 90 | Sugar free |
| 135 | 54 | M | 44 | 150 | 90 | 60 | Sugar in urine |
| 135 | 55 | | | 150 | 90 | 60 | Sugar free |
| 136 | 38 | M | 36 | 120 | 70 | 50 | Sugar in urine |
| 137 | 66 | F | 66 | 140 | 100 | 40 | Sugar in urine |
| 137 | 66 | | | 140 | 100 | 40 | Sugar free |
| 138 | 68 | F | 58 | 240 | 110 | 130 | Sugar in urine. Has nephritis |
| 139 | 50 | F | 48 | 220 | 70 | 150 | Sugar in urine. Aortic insufficiency |
| 139 | 50 | | | 210 | 50 | 160 | Sugar free |
| 139 | 51 | | | 200 | 50 | 150 | Sugar in urine |
| 139 | 51 | | | 200 | 50 | 150 | Sugar free |
| 140 | 38 | M | 36 | 140 | 100 | 40 | Sugar in urine |
| 140 | 39 | | 36 | 140 | 100 | 40 | Sugar free |

chronic nephritis or arteriosclerosis existed. He believed that the disease of itself is without influence on the arterial pressure.

Ehrmann[13] found that an existing acidosis in diabetics produced a low blood pressure an observation which I can confirm. Coader[14] reports a study of the blood pressure in twenty-seven cases of diabetes. Some of his cases were associated with albuminuria and some without albuminuria.

Some have thought that high blood pressures in diabetes were due to the high blood sugar, but this does not seem to be true.[15]

## II

### EXPERIMENTAL

The following tables containing the results obtained in my study of the blood pressures in one hundred and forty cases of diabetes mellitus, show the following:

1. The blood pressure in uncomplicated diabetes is normal or slightly under normal.

2. In every case in this series where there was present a high blood pressure there could be demonstrated that an existing nephritis, arteriosclerosis or aortitis was present.

3. In this series twenty-two cases of diabetes were complicated by hypertension—a percentage of about sixteen.

4. The presence or absence of sugar in the urine had no effect on the blood pressure.

5. A high blood pressure in diabetes is due to a chronic nephritis, arteriosclerosis or a cardiac hypertrophy.

## BIBLIOGRAPHY


[1]Potain: La pression arterielle de l'homme et l'etat normal et pathologique. Paris, 1902.
[2]Teissier: Gaz. d. Hôp., 1904, lxxvii, 1243.
[3]Vaquez: Gaz. d. Hôp., 1904, lxxvii, 1221.
[4]Hensen: Deutsch. Arch. f. klin. Med., 1900, lxvii, 438.
[5]Orr: Mont. Med. Jour., 1902, xxxi, 833.
[6]Goodman: Blood Pressure, 1914, p. 186.
[7]Elliott: Jour. Am. Med. Assn., 1907, xlix, 27.
[8]Joslin: The Treatment of Diabetes Mellitus, ed. 2, Philadelphia, 1917, p. 413.
[9]Kahn: Jour. Am. Med. Assn., 1920, lxxvi, 570.
[10]Crummer: Med. Herald, 1902, xxi, 46.
[11]Severie: Sem. Med., 1907, xxvii, 362.
[12]Janeway, T. C.: The Clinical Study of Blood Pressure, New York, 1904, p. 235.
[13]Ehrmann: Berl. klin. Wchnschr., 1913, l, 13.
[14]Coader: Valeur pronostique et diagnostique de la recherche systematique de la tension arterielle chez les diabetiques simples. Thèse de Paris, December, 1913.
[15]Port: Deutsch. Med. Wchnschr., 1913, xxxix, 69.

# THE COLLOIDAL BENZOIN REACTION OF CEREBROSPINAL FLUID*

By Fanny Warnock, A.B., Chicago, Ill.

As substitutes for the Wassermann and the Lange colloidal gold reactions as applied to cerebrospinal fluid, several tests have been proposed whose chief claims have been reliability equal to that of the above-named reactions and greater simplicity in the performance. It must be admitted that a test, which is at the same time easy to perform and reliable in its results, would have a wide field of usefulness. Of the proposed substitutes, which usually depend upon the flocculation of colloid suspensions, the mastic test has received the widest trial, without, however, results of sufficient uniformity to warrant its replacement of the more complicated procedures. The most recently proposed substitute is a flocculation reaction which makes use of a suspension of benzoin. Guillain, Laroche, and Lechelle[1] claim to have obtained with it results which parallel the Wassermann reaction, precipitation of the colloidal benzoin occurring only in certain tubes of the series in the case of syphilitic cerebrospinal fluid. They consider it more delicate than the gum mastic test and much less subject to error than the Lange colloidal gold reaction.

## TECHNIC

Only two solutions are required: a 1:10,000 solution of chemically pure sodium chloride in distilled water, and a suspension of benzoin resin. The latter is prepared as follows: 1 gram powdered benzoin resin is covered with 10 c.c. of absolute alcohol and allowed to stand for 48 hours. The clear liquid is then drawn off and 0.3 c.c. added gently to 20 c.c. of distilled water, then heated to 35° C. to insure a homogeneous suspension. Both solutions must be freshly prepared and the cerebrospinal fluid must contain no trace of blood.

In performing the test, 16 hemolysis tubes are set up in series and the fluids added according to the following arrangement:

| Tubes:— | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | c.c. | c.c. | c.c. | c.c. | c.c. | c.c. | c.c. | c.c. | c.c. | c.c. | c.c. | c.c. | c.c. | c.c. | c.c. | c.c. |
| Salt: | 0.25 | 0.5 | 1.5 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| C. S. fluid | 0.75 | 0.5 | 0.5 | | | | | | | | | | | | | 0.0 |
| Benzoin: | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | .1.0 |

The cerebrospinal fluid, as indicated, is added only to the first three Tubes. Then 1.0 c.c. is removed from Tube 3 and transferred to Tube 4, 1.0 c.c. from Tube 4 transferred to Tube 5 and so on to the fifteenth Tube, from which 1.0 c.c. is removed and discarded. Tube 16 receives no cerebrospinal fluid and serves as a control.

*From the Nelson Morris Memorial Institute for Medical Research of the Michael Reese Hospital. Received for publication, August 8, 1921.

The authors claim for the test that cerebrospinal fluid from patients with general paresis, tabes in evolution, or any diffuse syphilitic process of the nervous system precipitates the colloidal benzoin in the first nine Tubes of the series (sometimes the first thirteen). The flocculation always begins with the first tube of the series. This reaction in the first nine Tubes, in their experience, always paralleled the Wassermann reaction. Normal cerebrospinal fluids gave no reaction in the first five Tubes, though they admit that with a negative cerebrospinal fluid there may be precipitation in one or two Tubes of the series (Tubes 6 or 7). As a result of their work they considered flocculation in the first five Tubes characteristic and specific for syphilis and recently[2] have further simplified the test, as it relates to syphilis, by reducing the number of Tubes to four (the first being omitted) and a control. In an earlier communication[3] their results in tuberculous meningitis, using the full series of Tubes, are reported. For this condition they also claim a specific reaction, flocculation beginning at the upper limit of the syphilitic zone (Tube 6 or 7, sometimes Tube 4 or 5) and continuing to Tube 11 or on up to Tube 15.

Pauzat[4] has reported results based on the study of fifteen fluids. He found precipitation always feeble, sometimes absent, in the first Tube. With cerebrospinal fluids giving a positive Wassermann reaction there was precipitation up to the tenth Tube. Some of his spinal fluids with a negative Wassermann reaction gave partial precipitation, but never starting before the fifth Tube. He held that his results agree with the Wassermann reaction.

Huber[5] confirms the value of the test in replacing the Wassermann reaction. He cites instances where the clinical history indicated syphilis and the Wassermann was uncertain, but the colloidal benzoin was precipitated in the first five or six Tubes, that is, in the syphilitic zone.

If the results of these French observers can be confirmed, the colloidal benzoin reaction would be a simple procedure of great practical value. We have carried out the technic of the reaction, as given in the original communication of Guillain, Laroche and Lechelle,[1] on all the cerebrospinal fluids received in the laboratories of the Michael Reese Hospital during the past five months. In making up the 1:10,000 salt solution we have found it more accurate to prepare it from a 10 per cent solution of chemically pure sodium chloride, making only enough for the day's tests. The alcoholic solution of benzoin was made in quantity, the clear liquid drawn off at the end of 48 hours and preserved in a stoppered bottle. From this the benzoin suspension was made fresh each time. Whenever obtainable the cell count of the cerebrospinal fluid is recorded. For every case we have the results of the Wassermann, Lange colloidal gold, and Ross-Jones globulin reactions. We have arranged our results in two general groups; first, the cerebrospinal fluids from clinically syphilitic patients and all those fluids giving undoubtedly positive laboratory indications of lues; and second, the cerebrospinal fluids from non-syphilitic patients, fluids which give no laboratory evidence of syphilis.

### SYPHILITIC SPINAL FLUIDS

Of the syphilitic cerebrospinal fluids, Table I includes twelve from known syphilitic patients, where the Wassermann, Lange and globulin reactions

were all positive and the colloidal benzoin reaction could be regarded as characteristic for syphilis. Each of these showed precipitation of the benzoin suspension in the syphilitic zone comprised by the first five Tubes. Only one (105) began definitely in the first Tube; four (92, 93, 94, 120) were partly precipitated in the first Tube but not sufficiently for us to call them positive. Eight were negative in the first Tube. All but one (104) precipitated in Tube 3 and continued through the Tubes of the syphilitic zone. But none stopped with the fifth Tube, none before the ninth, and only one (113) before the thirteenth Tube. All but four continued to the thirteenth Tube. Furthermore, in a few instances precipitation occurred even in the sixteenth or control Tube, in which there was no spinal fluid at all.

In Table II are the cerebrospinal fluids where one or all the laboratory examinations certainly indicate syphilis while the colloidal benzoin reaction is negative in the first five Tubes. Two of these, (91 and 98) showed precipitation in the third Tube; two others (42 and 103) were partly precipitated in the third Tube; 103 gave partial precipitation on through the fifth, and 98 precipitated partly in the fifth Tube. None of these can be said really to begin before the sixth Tube, which according to the original article would be a negative reaction. Only one of these (103) did not continue through the thirteenth Tube; it stopped at nine. It might almost be called positive, were it not for the doubtful precipitation in Tubes 3 to 5, where it should be most marked.

TABLE I

SYPHILIS

| WASSERMANN OR LANGE REACTION POSITIVE. BENZOIN REACTION POSITIVE | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| LAB. NO. | DATE | DISEASE | CELL COUNT | ROSS-JONES | BENZOIN REACTION | | | | | | | | | | | | | | WASSERMANN | LANGE CURVE |
| | | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | | |
| 93 | 5/10 | Syphilis | | ++ | ± | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0 | ++++ | 5555542200 |
| 92 | 5/10 | Syphilis | | ++ | ± | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0 | ++++ | 5555555421 |
| 22 | 2/28 | Tabes | | ++ | 0 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | ++++ | 5555555200 |
| 105 | 6/3 | Syphilis | | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | ++++ | 5555533200 |
| 107 | 6/7 | Syphilis | | + | 0 | 0 | + | + | + | + | + | + | + | + | + | + | + | + | + | 0 | ++++ | 5555431110 |
| 113 | 6/10 | Syphilis | | + | 0 | + | + | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | ++++ | 5555443100 |
| 114 | 6/10 | Syphilis | | + | 0 | 0 | + | + | + | + | + | + | + | + | + | + | + | 0 | 0 | 0 | ++++ | 5555433300 |
| 136 | 3/24 | Syphilis | | + | 0 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | ++++ | 1111100000 |
| 50 | 3/21 | Syphilis | 10 | + | 0 | 0 | + | + | + | + | + | + | + | + | + | + | + | 0 | 0 | 0 | + | 1122332100 |
| 104 | 6/3 | Syphilis | | + | 0 | ± | ± | + | + | + | + | + | + | + | + | + | + | + | 0 | 0 | ++++ | 5555533322 |
| 94 | 5/10 | Syphilis | | ++ | ± | ± | + | + | + | + | + | + | + | + | + | + | + | + | ± | 0 | ++ | 5555532000 |
| 120 | 6/27 | Syphilis | | + | ± | ± | + | + | + | + | + | + | + | + | + | + | 0 | + | ± | 0 | ++++ | 1555555222 |

In this and the succeeding tables, the symbols under Benzoin Reaction indicate the following: 0, no change in the suspension. ±, partial flocculation; there is some precipitation but the supernatant fluid is cloudy. +, complete reaction; a heavy, white, flocculent precipitate settles to the bottom of the tube and the supernatant fluid is clear.

Table III comprises three cerebrospinal fluids where the clinical diagnosis was syphilis but where the laboratory findings were not confirmatory. The first (95), a case with a clinical diagnosis of cerebrospinal syphilis, gave negative Wassermann, Lange and globulin reactions. The cell count was only two lymphocytes. The second case (60) was under antiluetic treatment. The patient had had a chancre 25 years before. The Wassermann and Ross-

TABLE II

SYPHILIS

| WASSERMANN OR LANGE REACTION POSITIVE. BENZOIN REACTION NEGATIVE | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| LAB. NO. | DATE | DISEASE | CELL COUNT | ROSS-JONES | BENZOIN REACTION | | | | | | | | | | | | | | | WASS-ERMANN | LANGE CURVE |
| | | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | |
| 42 | 4/1 | Syphilis | 3 | 0 | 0 | 0 | ± | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | 0 | ++++ | 1112220000 |
| 98 | 5/28 | Syphilis | 2 | + | 0 | 0 | + | 0 | ± | 0 | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 5554210000 |
| 103 | 6/3 | Syphilis | | + | 0 | 0 | ± | ± | ± | ± | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | ++++ | 5555555433 |
| 111 | 6/10 | Tabes | 99 | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | 0 | 0 | ++++ | 0012200000 |
| 110 | 6/10 | Cerebral Hemorrhage | 35 | + | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | 0 | ++++ | 0011211000 |
| 91 | 5/10 | Syphilis | | + | 0 | 0 | + | 0 | 0 | + | + | + | + | + | + | + | + | + | + | 0 | ++++ | 5555532111 |

Jones tests were negative but the Lange curve could indicate cerebrospinal lues. The third (108) had syphilitic symptoms clinically, and the blood Wassermann reaction was three-plus positive. The cell count was normal, the spinal fluid Wassermann reaction was negative, the Lange curve changed no more than with some normal fluids. From Huber's observations the benzoin test should be most valuable in just such cases, but in none of the three did precipitation start before the sixth Tube. In all, precipitation continued through the thirteenth Tube and in two even through the sixteenth.

TABLE III

SYPHILIS

| CLINICALLY SYPHILIS. WASSERMANN REACTION NEGATIVE. BENZOIN REACTION NEGATIVE | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| LAB. NO. | DATE | DISEASE | CELL COUNT | ROSS-JONES | BENZOIN REACTION | | | | | | | | | | | | | | | WASSER-MANN | LANGE CURVE |
| | | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | |
| 95 | 5/25 | C. S. Lues | 2 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | 0 | + | + | + | 0 | 0 | 0 | 0 | 0000000000 |
| 60 | 2/23 | C. S. Lues | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | 0 | 0112110000 |
| 108 | 6/7 | Lues | 3 | 0 | 0 | 0 | 0 | 0 | 0 | ± | ± | 0 | + | + | + | + | + | + | + | + | 0 | 0011111000 |

The last group of syphilitic cerebrospinal fluids (Table IV) are from old treated cases where the laboratory results might not be expected to be strongly positive, or from cases where syphilis clinically was suspected but not certain, so that one might expect weak positives. In such cases, the benzoin reaction should be the decisive factor. In two cases (41, 43), where the Wassermann reaction was positive and the Lange curve slightly changed, there was precipitation beginning before the sixth Tube. Both of these partially precipitated in the first three and in the fifth Tubes. But what we record as partial could no more be included with the positives than it could be with the negatives. No clear precipitation appeared before Tube 7, except in one case (39) where the fourth tube precipitated, with nothing more till Tube 8. This, a treated case, had given a feebly positive Wassermann reaction. All but four continued through Tube 13. One case (14), a three-year-old child who died during an operation for cerebral tumor, had given a three-plus positive blood Wassermann reaction. The spinal puncture was performed after a month of mercurial treatment. The Lange curve was strongly suggestive of cerebrospinal lues and the lipoid antigen gave a

TABLE IV

SYPHILIS

SUSPECTED SYPHILIS AND TREATED CASES

| LAB. NO. | DATE | SYPHILIS | CELL COUNT | ROSS-JONES | BENZOIN REACTION | | | | | | | | | | | | | | | WASSERMANN | LANGE CURVE |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | |
| 43 | 4/1 | Treated Syphilis | 3 | 0 | ± | ± | ± | 0 | ± | ± | + | + | + | + | + | + | + | + | + | 0 | + | 1110000000 |
| 41 | 4/1 | Treated Syphilis | | 0 | ± | ± | ± | 0 | ± | 0 | + | + | + | + | + | + | + | + | 0 | 0 | ++ | 1111110000 |
| 39 | 4/1 | Treated Syphilis | | 0 | 0 | 0 | 0 | + | 0 | 0 | 0 | ± | + | + | + | + | + | + | + | 0 | + | 1112222000 |
| 112 | 6/8 | Treated Syphilis | 3 | 0 | 0 | 0 | 0 | 0 | 0 | ± | + | + | ± | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1111000000 |
| 38 | 4/1 | Treated Syphilis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | 0 | 0 | 0 | 0000000000 |
| 102 | | Syphilis | 4 | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | 0 | 0 | 0 | 0 | 0 | 0 | 2222211111 |
| 14 | 2/18 | Brain Tumor | 7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | 0123333000 |
| 117 | 6/22 | Early Paresis | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | (Blood Wassermann +++) 0000000000 |

one-plus positive reaction. Though the combined laboratory reports indicated syphilis, a glioma of the cerebellum was found at necropsy; there was no histologic evidence of luetic meningeal involvement. The colloidal benzoin precipitated in Tubes 9 and 10.

From our results on these twenty-nine syphilitic spinal fluids we come to the conclusion that the precipitation of colloidal benzoin in the first nine tubes of the series of sixteen is of no value in diagnosing syphilis for:

1. Precipitation beginning in the first five tubes of the series and continuing to the ninth and never going beyond the thirteenth, does not parallel the Wassermann or Lange reactions in unquestionably syphilitic fluids.

2. Precipitation in Tubes 1 to 9 does not confirm the clinical diagnosis of syphilis where the Wassermann and Lange test are negative or doubtful.

## NONSYPHILITIC SPINAL FLUIDS

The nonsyphilitic fluids are arranged in groups according to diseases. Table V shows the reaction of colloidal benzoin in parallel with the Wassermann and Lange reactions as carried out on fourteen meningitic fluids. Six cases of tuberculous meningitis showed precipitation between Tubes 6 and 14. Four out of the six continued to Tube 15. One (87) did not begin till the ninth tube. One (5) started with partial precipitation in Tube 3 and precipitated from Tubes 4 to 15. It was not different from the precipitation reaction of the syphilitic fluids in Table I. Another (11) precipitated throughout the series from 1 to 16. There seems to us to be no definite zone of precipitation with the tuberculous meningitic fluids.

Of two streptococcus meningitic fluids, one precipitated the colloidal benzoin in Tubes 6 to 14; the other gave partial precipitation in Tubes 3 to 6, then complete through the rest of the dilutions. Six spinal fluids from cases of meningococcus meningitis varied from the second to the sixth tube in starting the precipitation and from the twelfth to the sixteenth in stopping.

TABLE V

MENINGITIS

| LAB. NO. | DATE | DISEASE | CELL COUNT | ROSS-JONES | BENZOIN REACTION | | | | | | | | | | | | | | | | WASSERMANN | LANGE CURVE |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | | |
| 21 | 3/30 | Tuberculous Meningitis | 112 | ++ | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | 0 | 0 | 1122333300 |
| 19 | 4/1 | Tuberculous Meningitis | 112 | ++ | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | 0 | 0 | + | 0 | 0000233320 |
| 11 | 3/17 | Tuberculous Meningitis | 200 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | 1111220000 |
| 5 | 4/27 | Tuberculous Meningitis | | ++ | 0 | 0 | ± | + | + | + | + | + | + | + | + | + | + | + | + | 0 | 0 | 1112222000 |
| 85 | 4/29 | Tuberculous Meningitis | 182 | ++ | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | 0 | 0 | + | + | 0 | 0 | 0 | 0 | 0000000000 |
| 87 | 5/6 | Tuberculous Meningitis | | + | 0 | 0 | 0 | 0 | 0 | ± | 0 | 0 | + | + | + | + | + | + | + | + | 0 | 0001222210 |
| 4 | 3/23 | Streptococcus Meningitis | 4700 | ++ | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | 0 | 0 | +* | 1111222210 |
| 25 | 3/15 | Streptococcus Meningitis | | trace | 0 | 0 | ± | ± | ± | ± | + | + | + | + | + | + | + | + | + | + | | |
| 7 | 3/14 | Meningococcus Meningitis | | + | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 1111333221 |
| 9 | 3/30 | Meningococcus Meningitis | | + | 0 | 0 | 0 | 0 | 0 | ± | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0000123331 |
| 3 | 4/27 | Meningococcus Meningitis | | + | 0 | 0 | 0 | 0 | 0 | ± | + | + | + | + | + | + | + | + | + | + | 0 | 0011222455 |
| 81 | 4/27 | Meningococcus Meningitis | | + | 0 | ± | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0 | 0000001223 |
| 80 | 4/27 | Meningococcus Meningitis | | ++ | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0 | 0 | 1555555432 |
| 90 | 5/5 | Meningococcus Meningitis | | + | 0 | ± | ± | ± | + | + | + | + | + | + | + | + | + | + | + | + | 0 | 0011100000 |

*With cholesterinized antigen.

Six cerebrospinal fluids from epileptic patients (Table VI) all showed precipitation, but varied from Tubes 6 to 8 in starting and from 14 to 16 in stopping. One (88), starting with Tubes 6 and 7, precipitated every other tube to 15.

The fluids in Table VII, from five cases of encephalitis lethargica, are still more variable in precipitation. One (64) gave no precipitation; one (18) precipitated in Tubes 9 and 10; one (79) ran from 6 to 13 and one (83) from 7 to 14. One (46) precipitated Tubes 7 to 10, then alternated partial and complete precipitation on to the final Tube.

Table VIII shows the reaction with five fluids from cases of sclerosis. Number 6, a case of vascular sclerosis, precipitated Tubes 9 and 10; No. 2, a case of general arteriosclerosis, 7 to 9, with 12 partial; No. 23, multiple sclerosis, 7 to 11; No. 31, also multiple sclerosis, gave partial precipitation in Tubes 1, 2 and 7 and complete from 8 to 15; No. 37 gave continued precipitation only from 10 to 15; it was from a case of amyotrophic lateral sclerosis.

Table IX includes fifteen cases of nervous disorders and brain and cord lesions. These all gave negative Wassermann reactions and very slight change with the Lange test. Only two, a case of dementia precox (29), and a case of tetanus (32) were negative throughout. One started with the third Tube

TABLE VI

EPILEPSY

| LAB. NO. | DATE | DISEASE | CELL COUNT | ROSS-JONES | BENZOIN REACTION | | | | | | | | | | | | | | | | WASSERMANN | LANGE CURVE |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | | |
| 27 | 3/24 | Epilepsy | | . + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1111000000 |
| 28 | 3/24 | Epilepsy | | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | ± | + | + | + | + | + | + | 0 | 0 | 0 | 1111100000 |
| 30 | 3/24 | Epilepsy | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | 0 | + | ± | ± | + | 0 | 0 | 0 | 0000000000 |
| 35 | 4/1 | Epilepsy | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | + | | 1111100000 |
| 88 | 5/4 | Epilepsy | | 0 | 0 | 0 | 0 | 0 | 0 | + | + | 0 | + | 0 | + | 0 | + | 0 | + | 0 | 0 | 0000000000 |
| 78 | 4/27 | Epilepsy | | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | ± | ± | + | 0000111000 |

TABLE VII

ENCEPHALITIS LETHARGICA

| LAB. NO. | DATE | DISEASE | CELL COUNT | ROSS-JONES | BENZOIN REACTION | | | | | | | | | | | | | | | | WASSERMANN | LANGE CURVE |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | | |
| 18 | 2/15 | | | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0012210000 |
| 46 | 4/12 | | 28 | + | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | ± | + | ± | + | ± | + | 0 | 0011100000 |
| 64 | 4/1 | | 7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0122100000 |
| 79 | 4/27 | | 5 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0000000000 |
| 83 | 4/27 | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 1111100000 |

TABLE VIII

SCLEROSIS

| LAB. NO. | DATE | DISEASE | CELL COUNT | ROSS-JONES | BENZOIN REACTION | | | | | | | | | | | | | | | | WASSERMANN | LANGE CURVE |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | | |
| 23 | 3/24 | Multiple Sclerosis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | 1111100000 |
| 31 | 3/24 | Multiple Sclerosis | | 0 | ± | ± | 0 | 0 | 0 | 0 | ± | + | + | + | + | + | + | + | + | + | 0 | 0000000000 |
| 37 | 3/24 | Amyotrophic | | + | 0 | 0 | 0 | + | 0 | 0 | 0 | + | 0 | + | + | + | + | + | + | 0 | 0 | 0000000000 |
| 6 | 3/24 | Arteriosclerosis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0012211000 |
| 2 | 3/24 | Arteriosclerosis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | 0 | ± | 0 | 0 | 0 | 0 | 0 | 1112220000 |

and two with the fifth. Almost all precipitated in more than two or three tubes.

The normal cerebrospinal fluids, those from which one would not expect positive Wassermann or Lange reactions, are grouped together in Table X. Only one gave no precipitation with colloidal benzoin. Some showed precipitation in only one or two tubes, as the authors concede possible with a negative fluid, but most of them showed as much precipitation as some of the definitely syphilitic fluids. Number 82 was a case entered in the hospital under the diagnosis of auditory nerve deafness. The blood Wassermann was negative. The Lange was absolutely negative. The spinal fluid Wassermann was one-plus positive with cholesterinized human heart antigen and one-plus with syphilitic liver antigen in the incubator, but was negative with lipoid antigen and with syphilitic liver antigen incubated four hours in the ice box. There were no clinical symptoms of syphilis. The patient was discharged unimproved and readmitted a few weeks later. The blood Was-

sermann was again negative with all antigens. The Lange changed slightly in the first four tubes. The condition was diagnosed normal when discharged again. The cerebrospinal fluid from the second spinal puncture is given in the Table as 101. The benzoin test was done three times on 82 and once on 101. With 82, the first time there was precipitation in Tubes 7 to 14; the second time in Tubes 8 to 15 and the third time in 3 to 10 with partial precipitation in 11 and 13 as shown in the Table. With 101 there was precipitation in

TABLE IX

NERVOUS DISORDERS OR LESIONS OF BRAIN OR CORD

| LAB. NO. | DATE | DISEASE | CELL COUNT | ROSS-JONES | BENZOIN REACTION | | | | | | | | | | | | | | | | WASSERMANN | LANGE CURVE |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | | |
| 84 | 4/26 | Hydrocephalus | | | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | + | 0 | 0000000000 |
| 17 | 4/26 | Hydrocephalus | 3 | 0 | 0 | 0 | 0 | 0 | 0 | ± | + | + | + | + | + | + | + | + | + | + | 0 | 1111100000 |
| 86 | 4/17 | Lead Poisoning | 576 | + | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | + | 0 | 0 | 0000000000 |
| 115 | 6/15 | Hemiplegia | 5 | 0 | 0 | 0 | + | + | 0 | + | + | + | + | + | + | + | + | + | + | + | 0 | 0011110000 |
| 119 | 6/25 | Cerebral Thrombosis | 24 | 0 | 0 | 0 | 0 | 0 | + | 0 | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0122211000 |
| 99 | 5/25 | Cord tumor | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | 0 | 0 | + | 0 | 0 | 0 | 0 | 1111000000 |
| 20 | 4/ 6 | Chorea | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1111000000 |
| 97 | 5/28 | Pituitary Tumor | 10 | Trace | 0 | 0 | ± | 0 | 0 | ± | ± | + | + | + | + | + | + | + | + | 0 | 0 | 0011222200 |
| 89 | 5/ 2 | Neuritis | 2 | | 0 | 0 | 0 | 0 | 0 | ± | + | + | + | + | + | + | + | + | + | + | 0 | 1111333000 |
| 29 | 3/24 | Dementia Precox | | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1111100000 |
| 16 | 3/19 | Convulsions | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | ± | 0 | 0 | ± | 0 | 0 | 0 | 0 | 0 | 0 | 1111100000 |
| 33 | 3/24 | Cerebral Thrombosis | | ++ | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | 0 | 0012221000 |
| 118 | 6/25 | Poliomyelitis | 44 | 0 | 0 | 0 | 0 | 0 | + | 0 | + | + | + | 0 | ± | 0 | 0 | 0 | 0 | 0 | 0 | 0001210000 |
| 15 | 4/ 1 | Pernicious Anemia | | + | 0 | 0 | 0 | 0 | 0 | 0 | ± | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1112000000 |
| 32 | 3/24 | Tetanus | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0000000000 |

Tubes 5 to 7 only. Clinically, there was no thought of syphilis so we have put the case under normal fluids. But the one spinal fluid Wassermann, weakly-positive with two antigens, taken with the one weakly-positive Lange and the slightly increased cell count of twelve, from the laboratory standpoint were suggestive of syphilis. If the benzoin test were valuable for diagnosing syphilis it should be of value here. The one result, shown in the Table, of precipitation from Tubes 3 to 10 in 82 might confirm our suspicion of syphilis. Unfortunately, the benzoin reaction also gave two different reactions, precipitation beginning with Tubes 7 or 8. So in a case where it could be of assistance in a diagnosis it gave both a negative and a positive result.

In Table XI are grouped a few of those cerebrospinal fluids on which the benzoin test was repeated. The fluid from a case of tabes (107) was repeated once. Both times precipitation occurred in exactly the same tubes. Fluid from a case of lethargic encephalitis (83) precipitated first from Tubes 7 to 16, skipping 15; the second time from 7 through 16. A syphilitic fluid

TABLE X

CASES WITHOUT BRAIN OR CORD INVOLVEMENT

| LAB. NO. | DATE | DISEASE | CELL COUNT | ROSS-JONES | BENZOIN REACTION | | | | | | | | | | | | | | | | WASSER-MANN | LANGE CURVE |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | | |
| 101 | 5/9 | Normal | | 0 | 0 | 0 | 0 | 0 | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1111000000 |
| 45 | 4/6 | Normal | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | ± | ± | 0 | 0 | 0002220000 |
| 100 | 5/17 | Normal | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1111100000 |
| 96 | 5/17 | Normal | 24 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | 0 | 0 | 0000000000 |
| 106 | 6/6 | Normal | | + | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0000000000 |
| 109 | 6/7 | Normal | | 0 | 0 | 0 | 0 | 0 | 0 | ± | + | + | + | + | ± | 0 | 0 | ± | 0 | 0 | 0 | 0000000000 |
| 10 | 3/24 | Normal | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1111100000 |
| 12 | | Rachitis | | + | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1111100000 |
| 13 | 4/1 | Accident | | Trace | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1111100000 |
| 24 | 3/24 | Normal | | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0000000000 |
| 26 | 3/24 | Normal | | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | ± | + | + | + | + | ± | + | 0 | 0 | 0000000000 |
| 44 | 4/1 | Normal | | + | 0 | 0 | ± | 0 | 0 | 0 | + | 0 | + | ± | ± | ± | + | + | + | + | 0 | 0000000000 |
| 82 | 4/27 | Normal | 12 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | ± | + | ± | 0 | 0 | 0 | +* | 0000000000 |

*With Cholesterinized Antigen. Blood Wassermann negative.

(93) the first time precipitated Tubes 2 to 15, the second time only 5 and 6, then 9 to 14. Fluid from a patient with hemiplegia was set up three times at the same date to insure the solutions being the same. One test precipitated Tubes 7 to 16, the second precipitated Tubes 6 to 16 and the third precipitated 6 to 16 and Tubes 3 and 4 beside. A normal spinal fluid gave precipitation the first time in Tubes 7, 8 and 9 and the second time in Tubes 7 to 13. Number 92, a syphilitic cerebrospinal fluid with positive Wassermann, Lange and globulin reactions, showed precipitation, partly in the first tube and completely in the rest to 15. The second time it showed precipitation only in

TABLE XI

REPEATED BENZOIN REACTIONS

| LAB. NO. | DATE | DISEASE | CELL COUNT | ROSS-JONES | BENZOIN REACTION | | | | | | | | | | | | | | | | WASSER-MANN | LANGE CURVE |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | | |
| 93 | 5/10 | Syphilis | | ++ | ± | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0 | ++++ | 5555542200 |
| | 5/28 | | | | 0 | 0 | ± | ± | + | + | ± | ± | + | + | + | + | + | + | 0 | 0 | | |
| 92 | 5/10 | Syphilis | | ++ | ± | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 0 | ++++ | 5555555421 |
| | 5/28 | | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | 0 | 0 | 0 | 0 | 0 | | |
| 107 | 6/7 | Tabes | | + | 0 | 0 | + | + | + | + | + | + | + | + | + | + | + | + | + | 0 | ++++ | 5555431110 |
| | 6/10 | | | | 0 | 0 | + | + | + | + | + | + | + | + | + | + | + | + | + | 0 | | |
| 113 | 6/10 | Tabes | | + | 0 | + | + | + | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | ++++ | 5555443100 |
| | 6/15 | | | | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | |
| | 6/15 | | | | 0 | + | + | + | 0 | 0 | + | + | + | + | + | + | + | + | + | + | | |
| 111 | 6/10 | Tabes | | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | 0 | 0 | ++++ | 0012200000 |
| | 6/15 | | | | 0 | 0 | + | ± | 0 | 0 | + | + | + | + | + | + | + | + | + | + | | |
| | 6/15 | | | | 0 | 0 | + | 0 | 0 | + | + | + | + | + | + | + | + | + | 0 | 0 | | |
| | | Tuberculous | | | | | | | | | | | | | | | | | | | | |
| 5 | 4/25 | Meningitis | | ++ | 0 | 0 | 0 | 0 | 0 | 0 | 0 | ± | + | + | + | + | + | + | + | 0 | 0 | 0002222000 |
| | 4/27 | | | | 0 | 0 | ± | + | + | + | + | + | + | + | + | + | + | + | + | + | | |
| 83 | 4/27 | Encephalitis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | 0 | + | 0 | 1111100000 |
| | 5/6 | | | | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | + | | |
| | 5/6 | | | | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | ± | + | | |
| 115 | 6/15 | Hemiplegia | | | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | + | 0 | |
| | 6/15 | | | | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | + | + | | |
| | 6/15 | | | | 0 | 0 | + | + | 0 | + | + | + | + | + | + | + | + | + | + | + | | |
| 45 | 4/6 | Normal | | | 0 | 0 | 0 | 0 | 0 | 0 | ± | + | + | + | ± | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 4/8 | | | | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | ± | ± | ± | | |

10 and 11. The test does not seem reliable if the limits within which precipitation occurs may vary each time it is repeated.

The benzoin reaction was also carried out on several of our cerebrospinal fluids with 1:1000 sodium chloride solution instead of 1:10,000. This technic was taken from an English abstract.[6] The results were not different from those where 1:10,000 sodium chloride was used. There was the same variation with fluids from similar diseases and also the same variation when the test was repeatedly performed upon one spinal fluid. In this connection attention is called to the fact that in Guillain, Laroche and Lechelle's[4] latest modification of the test, distilled water is used instead of salt solution. Apparently the concentration of sodium chloride, when it varies within a range from nothing to 1:1000, has no bearing upon the discrepant results obtained.

## SUMMARY

In summing up the results of our experiments on the use of the colloidal benzoin precipitation reaction for cerebrospinal fluids we find:

That undoubtedly syphilitic cerebrospinal fluids do not regularly precipitate in any definite zone of dilutions.

That the benzoin reaction adds little in doubtful syphilitic cases.

That tuberculous meningitic cerebrospinal fluids do not precipitate the colloidal benzoin in any definite range of dilutions.

That many nonsyphilitic cerebrospinal fluids do precipitate the colloidal benzoin suspension, and even precipitate it in the so-called syphilitic zone.

That colloidal benzoin precipitation reactions repeated on the same fluid do not give uniform results.

Our results are based on tests performed on a total of 87 cerebrospinal fluids, twenty-nine of which were diagnosed syphilitic, either clinically or from the laboratory standpoint, and fifty-eight of which were nonsyphilitic. Of the twenty-nine syphilitic spinal fluids twelve precipitated in the syphilitic zone. Each of them continued beyond that range. Of the fifty-eight nonsyphilitic spinal fluids fifteen precipitated in the syphilitic zone.

## BIBLIOGRAPHY

[1]Guillain, G., Laroche, G., and Lechelle: Réaction de précipitation du benjoin colloidal avec les liquides pathologiques, Compt. rend. Soc. de Biol., Paris, July 17, 1920, lxxxiii, 1077.

[2]Guillain, G., Laroche, G., and Lechelle, P.: Technique simplifée de la réaction du benjoin colloidal pour le diagnostic de la syphilis de névraxe, ibid., June 4, 1921, lxxxv, 4.

[3]Guillain, G., Laroche, G., and Lechelle, P.: La réaction du benjoin colloidal dans la meningite tuberculeuse, ibid., Jan. 15, 1921, lxxxiv.

[4]Pauzat: Note sur la réaction de précipitation du benjoin colloidal dans le liquide céphalorachidien, ibid., March 12, 1921, lxxxiv, 503.

[5]Huber, J.: Contribution a l'étude biologique du liquide céphalorachidien au cours de la syphilis nerveuse par la réaction de précipitation du benjoin colloidal, ibid., March 12, 1921, lxxxiv, 496.

[6]Jour. Am. Med. Assn., January 15, 1921, lxxvi, 208.

# THE LABORATORY SPECIALIST AS A CLINICAL CONSULTANT*

By Wm. H. Bailey, A.B., M.D., Oklahoma City, Okla.

WHEN the author was invited by our Secretary to present a paper at this meeting on laboratory work he asked what phase of the subject he should choose. He was told that although some highly technical and little used test or some new and untried laboratory procedure might possibly be more interesting to the audience, still most of the profession would get more real benefit from the paper if it contained some practical points as to how to get the most out of the laboratory examinations that are in general use today and that have been found to be of value to the practitioner.

The three points that to the author's mind seem to give the best promise of getting the most out of the laboratory examinations in general use today are: (1) to consider all laboratory findings as clinical symptoms, (2) to decide which tests you are going to make in your office laboratory and then select some laboratory to do your more time-consuming and technical examinations, (3) to call in the pathologist as a clinical consultant in the obscure cases, except where the examinations are made as a routine.

Probably the most important point of all is the first, that laboratory findings must be considered simply as additional clinical symptoms. They should only be used to assist in establishing or excluding a diagnosis and not to make a diagnosis by themselves. A single negative examination of any specimen is of no value, especially if the other clinical symptoms do not agree with it. Even a positive result must have clinical evidence to support it. The laboratory findings must check with the other clinical findings. This fault of depending too much on the laboratory findings to make a diagnosis is probably the result of the attitude of the laboratory workers as much as it is the internists. In laboratory work, as in most every other line, a little knowledge is a dangerous thing. Laboratory findings are usually so definite that the poorly prepared or unthinking laboratory worker is inclined to think that they are all in all. The more time and study given to laboratory results as clinical symptoms the more correct will be their interpretations, and the more value they will be to the profession.

The second point, that of deciding which examinations you will make in your office laboratories and which you will send away to some larger laboratory is scarcely less important than the first. Perhaps all of you do not realize that to fully equip a modern laboratory requires as much investment as to fit up a well appointed office or the operating room of a well equipped hospital. Many of the tests that we are called upon to make today, as the Wassermann reaction, the various blood chemical examinations, etc., require several hours

*Read before the Southwest Medical Association, at Wichita, Kansas, Nov. 23, 1920.
Received for publication, June 19, 1921.

of continuous operations so that on account of the time element alone the general practitioner should not attempt to do them. Many of the tests require special training along the lines of chemistry, bacteriology and pathology, considerably above the amount most of us possessed at the time we graduated from a medical school. The busy practitioner does not have time to acquire this special training unless he can go away for postgraduate study frequently.

There are some laboratory examinations which, on account of their nature, have to be made immediately on the specimen's being collected from the patient. Examinations of this class are the coagulation time of the blood, test for per cent of hemoglobin, darkground examinations for spirochetes in primary venereal sores, feces examinations for ameba, cell counts in spinal fluids, etc.

There is a second class of examinations which can be made at some time after the collection of the specimen, within an hour or so. This class includes red and white blood cell counts, etc.

A third class, which is probably the largest, can be examined at any time within a reasonable period after the collection of the specimen. The equipment necessary for the examination of many of these is not very elaborate. They can be examined by the physician in his office but it is usually more satisfactory to send the majority of them to some other laboratory for examination. In this class we have differential white cell count, examination of sputum for tubercle bacilli, examination of various exudates for bacteria, routine examination of urine, blood smears for malaria, etc.

A fourth class includes those examinations which require more elaborate equipment and considerable time to complete them, and which are more satisfactory if sent away to some other laboratory. This class includes the Wassermann test on blood and spinal fluid, culture work for autogenous vaccines, gold chloride test on spinal fluid for cerebrospinal infections, examination of tumors for malignancy, the tests of the newer blood chemistry, etc.

It will readily be seen that unless the physician does those laboratory examinations coming in the first group himself, or is able to have a laboratory man visit his patient, he will not be able to gain the help that can be gotten from them.

Just how many of the examinations in the other three groups he does will depend upon how much time he will be able to give and what equipment he has at his command. Much depends upon the proper equipment, such as standard solutions and stains, and these usually deteriorate on standing, even if tightly corked. The doing of the various tests frequently enough to keep one's self efficient in the technic and familiar with the findings is essential. Even one who is used to spending a large part of his time in laboratory work finds that it is necessary to keep in training, as it were, in order to be sure of his results. Therefore, it is much better to have your office equipped to do only certain tests and to send the remainder of your work to some laboratory.

It will be seen in this outline that unless the physician is able to have a laboratory man visit his patient and collect the specimen, it is necessary for

the clinician himself to be informed as to how best to collect the specimen and transport it to the laboratory so as to give the pathologist the best opportunity of gaining the information he desires. Much could be said on this point alone, but such details will have to be omitted at this time.

The doctor submitting the specimen should understand in a general way how it is to be examined, that is, he should know the principle of the test and the general steps in the technic. By this knowledge he will appreciate in just what shape the specimen should reach the laboratory. Often the most important part of the whole examination is defeated because the specimen has not been secured in the proper way or safeguarded properly while en route to the laboratory.

The last point that we wish to make, that of using the pathologist as a clinical consultant, although possibly a new idea to some, is nevertheless an important one, if we are going to get the most out of laboratory work. Perhaps some do not realize, until they stop to think, that there are today many graduate physicians who have gone into laboratory work and who have been limiting their practice to this specialty for the last five to ten years. We believe that it can be said in their favor that as a class they stick more closely to their special line than do some of the men in other fields of specialization. If a doctor hopes to get anywhere in the laboratory game today it will take his whole effort and energy and he will not have time to practice in other fields in which he is not competent.

In spite of the large amount of pay work that is done free of charge by state laboratories, thanks to the loyal support of the profession of the southwest there are many fully equipped laboratories in this section of the country, with a graduate physician in charge, limiting his practice to laboratory work. No one should try to make you believe that it requires an M.D. degree to make a Wassermann test properly. Many of our best bacteriologists are not graduate physicians. You cannot deny that some, or possibly most, recent great advances in laboratory work have been made by men outside the medical profession. It is not our desire to detract from the value of the laboratory work when done by a nurse, a technician, or a laboratory assistant. They are valuable and absolutely necessary and frequently become more skillful than many medical men who are doing this line of work. We need more of these trained assistants; yet when it comes to interpreting a laboratory result as a clinical symptom a degree in medicine and in addition several years' experience as a general practitioner, cannot help but be of some assistance.

A few instances from our experience may assist in emphasizing the points that we have outlined.

Practically every man who has done much laboratory work has repeatedly been told by some doctor when he has submitted a specimen, say of blood for a Wassermann reaction, that this patient has been to see half a dozen other doctors, has had several Wassermann tests run by different laboratories, reports from which did not always agree, and that he wants you to test it very carefully so that he can know definitely whether this patient has or has not syphilis. It cannot be done by a Wassermann test alone and it

should not be expected. Although a 4-plus positive is strong presumptive evidence of syphilis, even such a result should not be taken alone as a positive diagnosis. Many cases of syphilis do not give a positive Wassermann at the time the blood happens to be taken; this is especially true in the early primary, the tertiary stages, and in cerebrospinal lues.

You will appreciate the uselessness of a single negative examination for tubercle bacilli in sputum. The time to diagnose pulmonary or laryngeal tuberculosis is before the bacilli appear in the sputum. Of course often the patient does not present himself for examination during this incipient stage.

Throat smears or cultures for diphtheria are difficult to take, especially in young children, and a negative examination should be disregarded if the history of exposure, and especially the clinical symptoms, are at all suspicious.

Examples of similar nature might be added indefinitely but perhaps those given are sufficient to illustrate our point, that laboratory findings are always to be taken simply as clinical symptoms.

The careful pathologist should always take time to collect a brief history of the case and make a physical examination whenever the opportunity presents. With material that is sent in from the outside or through the mail by the doctor there should always be sent a summary of the history and clinical findings. This data is often of the greatest value in assisting the laboratory man in making correct "interpretations" of his results. Some may say if the laboratory man knows what the doctor is looking for it is likely to prejudice his interpretation. This should not be the case with a laboratory consultant any more than it is with a consultant in any other line of specialty. We doubtless know of doctors doing large consultation practice who never disagree with the doctor on the case and so stand in well with them. Such relations and methods may be all right from a financial standpoint, but such men are not practicing medicine.

A review of a few cases may show more clearly what we mean by this closer co-operation between the doctor and the laboratory and the use of the laboratory man as a clinical consultant.

A specimen of blood received in a vacuum bleeding tube, from Doctor M., with a request for a Wassermann and blood count. In a letter accompanying the specimen the doctor gave a history of the case stating that the patient had been losing weight slowly for a couple of years, that he appeared anemic and that there was a definite tumor palpable in the upper left abdomen, which moved with respiration. He stated that he suspected syphilis or malignant tumor. The Wassermann was made and found a 2-plus positive. I could not make a blood count as requested as most of the cells are bound up in the fibrin clot when blood is collected in a tube. Even in the face of a 2-plus positive, which I reported, I believed the case showed many symptoms of leukemia. Occasionally a weak positive Wassermann is given in these cases. I suggested that a white cell count be made. This was done and showed a leucocyte count of over 200,000, which of course completed the diagnosis.

A throat smear and culture from a suspected diphtheria case were submitted, the direct smear was negative for diphtheria as was also the culture

the next morning. On inquiry as to the symptoms of the case I was informed that the child had a temperature of 101-102° for a few days, pulse 110-115, considerable prostration and one nostril had been completely closed for several days and was discharging a slight amount of secretion. I stated that antitoxin was indicated and requested separate cultures from the nose and throat, both of which showed diphtheria positive.

A third case was one in which I was asked to go out to take blood for a Widal. As is the custom I questioned the patient as to his history and present symptoms, and made a brief physical examination. I found that he had had a fever for about a week with a few slight chills at irregular periods. His abdomen was soft and flat with no tenderness in the iliac regions but distinct tenderness and a dull aching pain in the right lumbar region. A white cell count and blood smear for differential count were taken at the same time the Widal was collected, a specimen of urine was also requested. The Widal was negative, the white blood count was 15,400 with 85 per cent polys. and the urine was loaded with pus. I reported that the laboratory findings pointed to some pus infection in the genitourinary tract and suggested that the ureters be catheterized. This was done and a large pus kidney on the right side was discovered.

In conclusion I wish to quote a point that was brought out in a recent article in the *Journal of the American Medical Association* which in my opinion was most timely. The statement was as follows: "It should be emphasized that a knowledge of the laboratory and its standards, technic, and method of reporting is more important in obtaining the information desired than the reports obtained from a number of different laboratories which may not be careful or accurate. In other words it is the clinician's duty to know the possibility of error in the laboratory he is using. It is much better to have a test repeated several times in a laboratory to whose technic one is accustomed than to have a single test made in several laboratories which will only lead to confusion."

## DISCUSSION

*Dr. C. D. Blachly, Drumright, Okla.*—Of all the various kinds of laboratory work being done these days possibly a certain list of them can well be done by the general practitioner and should be done by him. On the other hand there is a certain list of examinations which usually can either not be done at all or only under great disadvantage.

Taking our own office as an example, since we do not try to specialize in laboratory work but only do that which can be routinely done on our patients, the first list should include red and white blood counts, and differential white blood counts, hemoglobin estimation, direct smear examination of exudates and spinal fluids, examination of blood for malarial plasmodium (more satisfactorily done on fresh unstained blood at the bedside or in office than to make blood smears and refer to distant laboratories) urinalysis, chemical and microscopical; stomach contents, chemical and microscopical; dark ground and stained smears for Spirochete pallida and feces examination, chemical and microscopical.

The second list which we do not try to do in our office, includes Wassermann tests on blood and spinal fluid, globulin and gold chloride on spinal fluid; tissue diagnosis of tumors, etc.; cultural examinations of throat smears for diphtheria; animal inoculations; blood chemistry, etc.

I wish to emphasize Dr. Bailey's point about the laboratory being a means of eliciting clinical symptoms and signs quite on a par with all other forms and means of diagnosis.

*Dr. E. A. Peterson, Denver, Colo.*—There has been a decided tendency on the part of some in the last year or two to discredit the findings of the laboratory and to place an overdue amount of emphasis on the clinical examination. Some probably gathered this idea from Dr. Pottenger's paper in which he stressed so vigorously the careful examination of the patient in the diagnosis of early tuberculosis. All of us who know of Dr. Pottenger's work, know that he is just as thorough and insistent on every other phase of an examination as he is on the clinical phase.

I like to regard my office as being divided into three laboratories; each of which is just as essential as any other, and without any one of which we have not given our patient the full measure of our knowledge. The physical and clinical examination of the patient I would say is done in the clinical laboratory. Then follows the x-ray examination in the x-ray laboratory and this is followed by the chemical and bacteriological analysis made in this laboratory; and I try to pass the patient through each of these laboratories in every case in which the diagnosis is at all obscure. We frequently find more satisfactory results from the clinical laboratory, whereas, in other cases, the chemical or x-ray laboratory may give us a diagnosis of tuberculosis in which the mere findings of the tuberculosis bacillus in the sputum will decide for once and for all that the patient has tuberculosis, and I want to stress here the point that so frequently the diagnosis of tuberculosis is not made in its incipiency because physicians are being taught that the tubercular bacillus does not occur until a later stage. If the patient were examined, in every case of suspected tuberculosis, as soon as it is suspected, and the proper treatment carried out just as soon as the bacillus can be demonstrated, I feel that the majority of cases of tuberculosis would get well.

It has been my experience in questioning patients, that the sputum examination has usually been put off until the patient is in the second or third stage of the disease. The reason for this is that the incipient stage, to which specialists refer as not showing tubercular bacilli in the sputum, is hardly regarded as a case of sickness by the average practitioner, and I believe that the majority of cases reach the second or third stage within a few weeks after the inception of the disease. So there is no reason at the present time to hesitate to examine the sputum for tuberculosis in any suspected case, and to repeat the examination if the sickness continues and the bacilli are not found at the first examination.

*Doctor Logan Clendening, Kansas City, Missouri.*—Doctor Bailey has referred to the desirability of the clinical pathologist's practicing his specialty as a specialty. I agree to this, but find practically, at least in the community where I live, that the pathologist is usually engaged in some clinical side line, such as syphilography, or is working towards clinical practice and using clinical pathology as a stepping stone. I do not particularly blame him as the fees for doing clinical pathology compared to the fees for doing x-ray work, a sister laboratory specialty, or giving salvarsan injections are entirely too small. But I do deplore the fact. Clinical pathology of a right, ought to be an end in itself. The solution for the problem I believe to be in the employment by hospitals of clinical pathologists who will receive adequate compensation, and will be allowed to work out the problems of their specialty in the hospital's laboratory. Under these circumstances he will be called in, as a consultant, by the physicians of the hospital not only in their hospital cases but also in their general practice.

*Dr. J. H. Stokes, Rochester, Minn.*—I wish to express my appreciation of the valuable points raised by Dr. Bailey. One has only to work in association with a large group of men to appreciate the possibilities of the laboratory man as a consultant. I feel the laboratory expert is as much entitled to do his work in the light of all the findings in the case, as is the clinician. I suggest, however, that the laboratory man in his turn should be on his guard against the *ipse dixit* frame of mind which would lead him to feel that the laboratory was the court of last resort, and that his decisions have the value of absolute truth. The laboratory findings should only be regarded as part of the clinical evidence, and in the end judgment must rest upon the whole of the facts and not upon any one part. I feel that it is not out of place to emphasize that the laboratory expert should have a wholesome respect for clinical judgment particularly as to the need for certain special

examinations. I have known of laboratory men who have presumed to inform the clinical expert as to whether or not the examination called for was indicated and have even declined to perform it in the absence of any contraindication except their own opinion that it was unnecessary.

I feel that the laboratory expert is at his best in the midst of the group of clinicians with whom he works and that geographical separation of clinic and laboratory, inevitably works to some extent to the disadvantage of both.

*Dr. R. H. Needham, Fort Worth, Texas.*—It is of utmost importance that the laboratory director be a graduate physician and he should avail himself of a pathologist as a consultant, placing all clinical data before him. The pathologist should feel free to suggest and to carry out, if necessary, any laboratory work which he thinks might be of value in working out the case. One should never make the rather common mistake of consulting the pathologist and then passing over his suggestions. Teamwork is absolutely essential.

The physician should decide just what tests he wishes to perform in his office laboratory. In reaching this decision, he should be governed by his ability, equipment, time and assistance for such work. Office tests are of little value unless efficiently performed.

The more complicated tests should be sent to a larger laboratory. From my own experience as a laboratory worker and physician, I am certain that it is more profitable and satisfactory to select one laboratory for work. The doctor should try to become intimately acquainted with the laboratory staff. Also take time to discuss and view tests, technic, etc., and become familiar with the per cent of error. If more than one individual performs the Lange or Wassermann tests study and compare their work and it may surprise one how the so-called errors and discrepancies may disappear.

I do not approve of sending duplicate tests to several different laboratories. First, it is not just; second, it usually but adds to the confusion. Stick to one laboratory until convinced that the work is not up to standard. Above all, study and become familiar with the different laboratory tests and technics, in order to be able to intelligently conclude or criticize. One must know what is the standard of work in a laboratory, if the laboratory specialist is to be of value as a clinical consultant.

*Dr. Bailey* (closing the discussion).—The best arrangement is, of course, in the group practice idea where if there is a pathologist at the head of the laboratory, as there should be, he will be called in frequently as a consultant and will have access to all the other clinical evidence to assist him in making correct interpretation of his laboratory findings. If by this relationship the group is able to do more accurate and scientific work, so also can the single practitioner do better work and get the most out of the laboratory, by placing himself in close association with the laboratory.

# *LABORATORY METHODS*

## A METHOD FOR PRODUCING A SPINAL DOG*

By J. Earl Thomas, M.D., St. Louis, Mo.

FOR many purposes in experimental physiology and pharmacology a spinal animal furnishes the most satisfactory preparation. Methods for preparing such an animal as well as methods for decerebration of animals are described by Sollman.[1] References to the literature will also be found in his book. An additional method is described by Jackson.[2]

These methods may be classified as (*a*) cutting operations in which the cord is severed below the medulla, with or without destruction of the higher parts of the brain; (*b*) methods of producing anemia of the higher centers by ligation of the vessels or injection of inert materials which block the blood vessels; and, (*c*) elimination of the brain by injecting poisons, usually chloroform, into its circulation.

In the method to be described an effort has been made to combine the the advantages of two of these methods (*b* and *c*). It consists essentially of injecting a mixture of chloroform and petrolatum into a carotid artery after ligating the other carotid and both vertebrals. When properly done this produces a spinal animal without convulsions or rigidity and apparently without shock.

In detail the method is as follows: The animal (dog) is etherized and tied down, belly up, in the usual way. The trachea is exposed and prepared for artificial respiration. Both carotids are secured and one is ligated. The ligated vessel will be available for blood pressure determination. Both vertebrals are secured and tied. The dissection for exposing the vertebrals to view, if this is thought necessary, is described by Sollman, p. 280,[1] and Jackson, p. 195.[2] Excellent drawings illustrating the dissection are shown by Jackson on the two preceding pages. With a little practice it will be found unnecessary to expose the vertebral arteries as these can be easily located with the finger passed down along the carotid sheath to the origin of that vessel. The origin of the vertebrals may be felt just a little lateral to the carotids and their identity verified by tracing them to the point where they enter the lateral processes of the cervical vertebrae. Their extensibility will permit them to be drawn up and ligated without extensive dissection.

The materials and apparatus for the injection consist of chloroform, vaseline, a 25 c.c. graduated cylinder, a large syringe with a large needle, and a means of warming the vaseline and the apparatus. For this purpose a little

*From the Physiology Laboratory of St. Louis University School of Medicine, St. Louis, Mo.
Received for publication, June 9, 1921.

water, heated in any convenient vessel is satisfactory. The vessel containing the petrolatum, and the syringe, needle, and cylinder are placed in the water to warm while the animal is being prepared for the injection.

To prepare the mixture, from 3 to 5 c.c. of chloroform are placed in the cylinder and followed by enough melted vaseline to make 20 c.c. and the mixture shaken. It is then drawn into the syringe and immediately injected into the unligated carotid. The injected mixture, which can be seen through the vessel wall, will at first be carried away from the point of injection by the circulating blood. After a certain amount has been injected the pressure of the blood will no longer be sufficient to force the mixture ahead and it will begin to back up in the carotid between the point of injection and the heart. When this occurs the carotid is clamped firmly with a hemostat proximal to

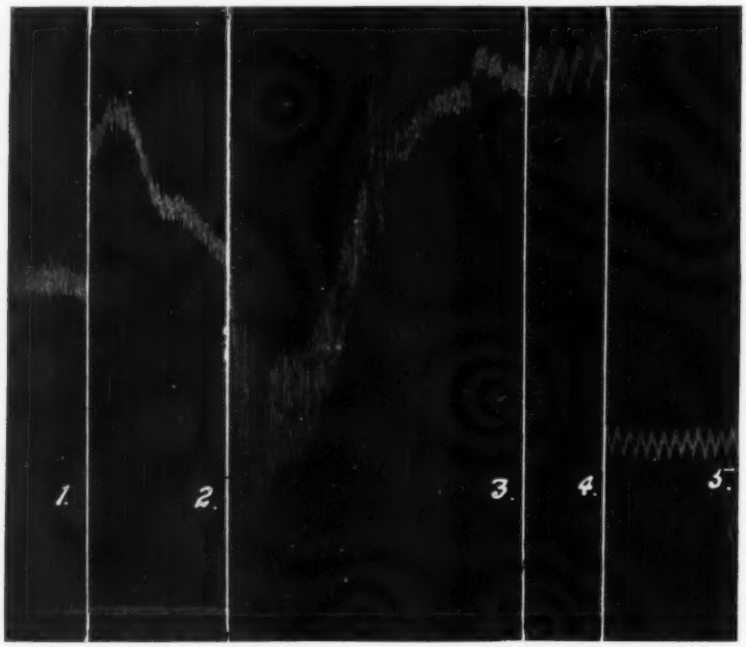


Fig. 1.—Record of the blood pressure of a 40 kilo dog during and immediately following the injection of a mixture of chloroform and vaseline into the carotid artery by the method described in the text. (1) Blood pressure under ether, before injection. (2) Rise and fall just after beginning the injection. (3) Blood pressure just before completing injection. Strong vagus action which passes off rapidly. (4) Injection completed, artificial respiration begun. (5) Blood pressure five minutes after completing the injection.

the needle and the injection continued. The respiration will cease about this time. A few c.c. should be injected after the respiration has stopped to insure against recovery. Considerable force may be safely used in completing the injection. The carotid is ligated distal to the needle before it is withdrawn to prevent escape of the mixture through the needle hole. Artificial respiration is begun whenever necessary.

During the injection the animal is likely to behave as follows: With the beginning of the injection there is a marked increase in the respiration and a considerable rise in the blood pressure. As the injection progresses this is followed by slowing and stoppage of the respiration and a fall in the blood

pressure with a very slow heart, due apparently to powerful vagus stimulation. This condition is alarming but has never proved fatal to the animal. Artificial respiration should of course be started at once. The heart may come to a complete stop but recovers promptly and the blood pressure then goes very high with no further evidence of vagus action. The condition of the heart as shown by its ability to maintain this high blood pressure as well as its recovery from the strong vagus action may be cited as evidence that chloroform does not get through to the venous circulation in dangerous amounts. The injection is usually completed soon after the vagus effect has passed off and the blood pressure then falls gradually until it reaches the level characteristic for spinal dogs. This series of events as it affects the blood pressure is shown in Figure 1. In many experiments the blood pressure has remained at nearly a normal level for an hour or longer though no evidence of a surviving medulla could be obtained. Blocking of the cerebral vessels and the consequent transference of a large amount of blood from the head to the remaining circulation may be a factor in keeping up the blood pressure.

In using this method, or any method other than actual section of the cord,

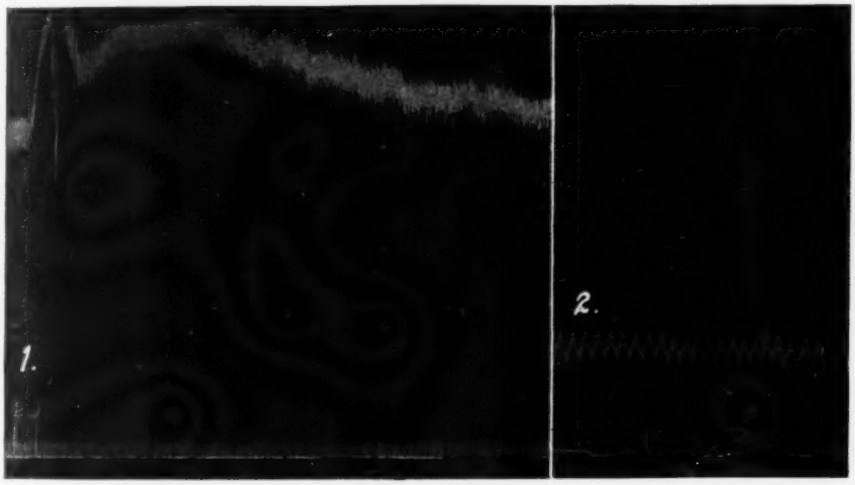


Fig. 2.—Effect on blood pressure of stimulating the central end of the left cut vagus before and after injecting chloroform-vaseline mixture into the right carotid. (1) Sharp rise in pressure with reflex slowing of the heart before injection. (2) After completing the injection. No effect.

the question will come up of whether or not the medulla is really excluded by the procedure. Several methods may be used to determine this point. All will depend on whether or not reflexes may still be obtained through the medulla. The simplest method perhaps is to observe the effect of stimulation of the central end of a cut vagus on the blood pressure. No effect will be produced in a spinal animal. Another method is to raise the blood pressure by any convenient means. If the medulla is intact there will be compensation with an evident effort to return to normal. Figures 2 and 3 illustrate the application of these methods of determining the absence of a vasoreflex mechanism. Figure 2 shows the effect of central vagus stimulation before and after injection. Figure 3 shows the degree of compensation before and after injection for a rise in blood pressure produced by equal doses of epinephrin.

The method may also be used to produce a functionally decerebrate animal by omitting the ligation of the vertebrals and stopping the injection as soon as the mixture ceases to be carried away by the blood stream, in other words, injecting at a pressure not higher than the blood pressure. For this purpose the mixture must be injected very slowly, consuming approximately five minutes in injecting the 5 or 10 c.c. that will be required for the purpose. The injection must of course be stopped and the vessel clamped if the respiration shows embarrassment. An animal so treated will usually remain quiet and live indefinitely if the temperature is artificially maintained. Death from hyperpyrexia is an occasional accident, though as a rule the temperature falls. This modification is not suitable for work in which the central nervous system is a factor because of the very obvious uncertainty as to the exact limits of

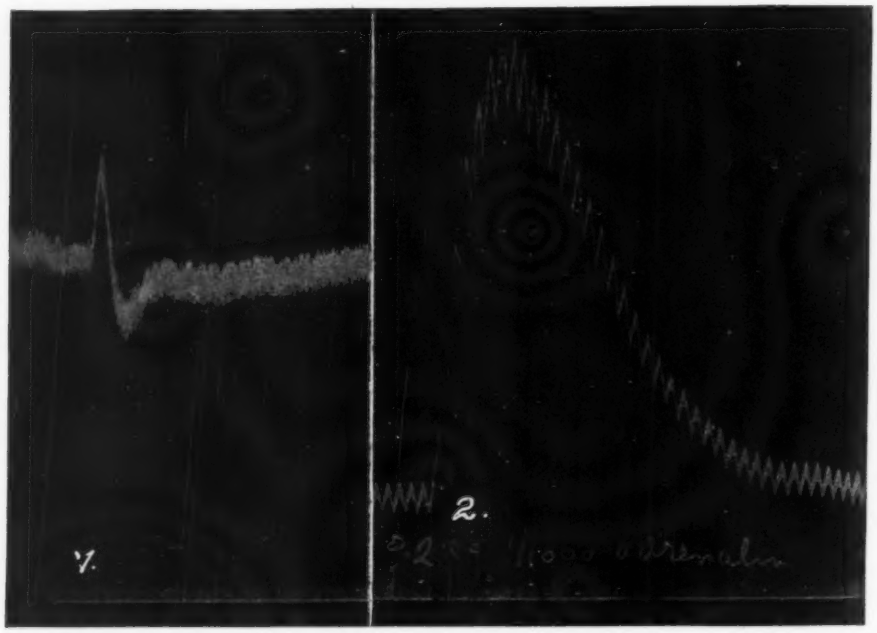


Fig. 3.—Effect on blood pressure of injecting 0.2 mg. of epinephrin intravenously (40 kilo dog) before and after destroying medulla with chloroform-vaseline mixture as described in the text. (1) Overcompensation when medulla is intact. (2) Apparent absence of compensation showing that the reflex function of the medulla has been eliminated.

the destruction produced. Means for artificial respiration should be at hand during the injection as temporary failure of the respiration is not an uncommon occurrence.

This method was devised in the Physiology Laboratory of St. Louis University School of Medicine and first used successfully in demonstrations in connection with the class work in pharmacology at that institution. It has also been used by Dr. Homer Wheelon and myself in an investigation of the pharmacology of nicotin, the results of which have not yet been published.

REFERENCES

[1]Sollman, Thorald: A Laboratory Guide in Pharmacology, Philadelphia, 1917, W. B. Saunders Co., p. 160.
[2]Jackson, Dennis E.: Experimental Pharmacology. Mosby, St. Louis, 1917, p. 195.

# A SPIROMETER FOR CONTINUOUSLY AND AUTOMATICALLY MEASURING EXPIRED AIR AND SAMPLING FOR ANALYSIS*

By Charles Claude Guthrie, M.D., Ph.D., Pittsburgh, Pa.

THE apparatus consists of two identical bell spirometers, mounted together and connected so that the expired air can be switched from one to the other without interfering with the respiration of the subject. While one is filling the other is sampled and emptied.

*Form I.*—This form has been employed for studies on dogs. The bells have a capacity of fifteen liters each. The anesthetized animal is connected by a tracheal tube with the anesthetic bottle and respiratory valves.[1] The expiration valve is connected by a tube to the spirometer. Room air is drawn through the anesthetic container and expelled into the spirometer automatically. The expired air is directed to one or the other spirometers by turning the tap by hand. When one is filled the tap is turned to switch the expired air to the other and the amount of air collected and time occupied, noted and recorded. A sample is taken for analysis and the bell emptied while the other is filling. With this method as with all other methods based upon the collection and analysis of expired air, when a volatile anesthetic is employed it becomes a factor in the analysis.

*Form II. Fig. 1.*—The general plan of the apparatus is the same as Form I, the essential differences being, (1) The bells are directly counterpoised, one against the other so that filling and discharging are continuous. The working capacity of each is five liters. (2) Switching the air from one to the other is entirely automatic. This is accomplished by a four way tap (Fig. 2), turned by a weight and controlled by a quadrant stop (Fig. 3). Two triggers control the stop and are worked by a double horizontal lever which in turn is moved by the bells pushing upward on the outer ends. The levers are adjusted to pull the triggers when five liters of air are introduced. (3) An indicator automatically records on a dial the total amount of air expired in five liter units, up to 180 liters and repeats without adjustment (Fig. 1, No. 13 and Fig. 4). (4) An automatic sampling device (Figs. 1, 5 and 6). This consists of an expired air chamber, an adjustable siphon and a pressure stabilizer, which at a regular rate draws one per cent, or more or less as desired, of the discharged air into a receiver for analysis. (5) Means are provided for conveniently and rapidly saturating the liquid used in the sample receiver with the subject's expired air before the sample is taken.

Taps are provided for drawing samples from either spirometer directly as in Form I.

*From the Department of Physiology and Pharmacology, School of Medicine, University of Pittsburgh.

Received for publication, July 23, 1921.

SAMPLE RECEIVER

This consists of a 500 c.c. narrow necked glass bottle. (Fig. 1 No. 7.) The neck is ground and fitted with a rubber stopper. The stopper is pierced with three holes. In one of these is fitted a piece of glass tubing so that the lower end is flush with the small end of the stopper. Into the other holes are fitted longer tubes which extend to near the bottom of the bottle. The lower end of one of these tubes is drawn to a narrow point and turned sharply

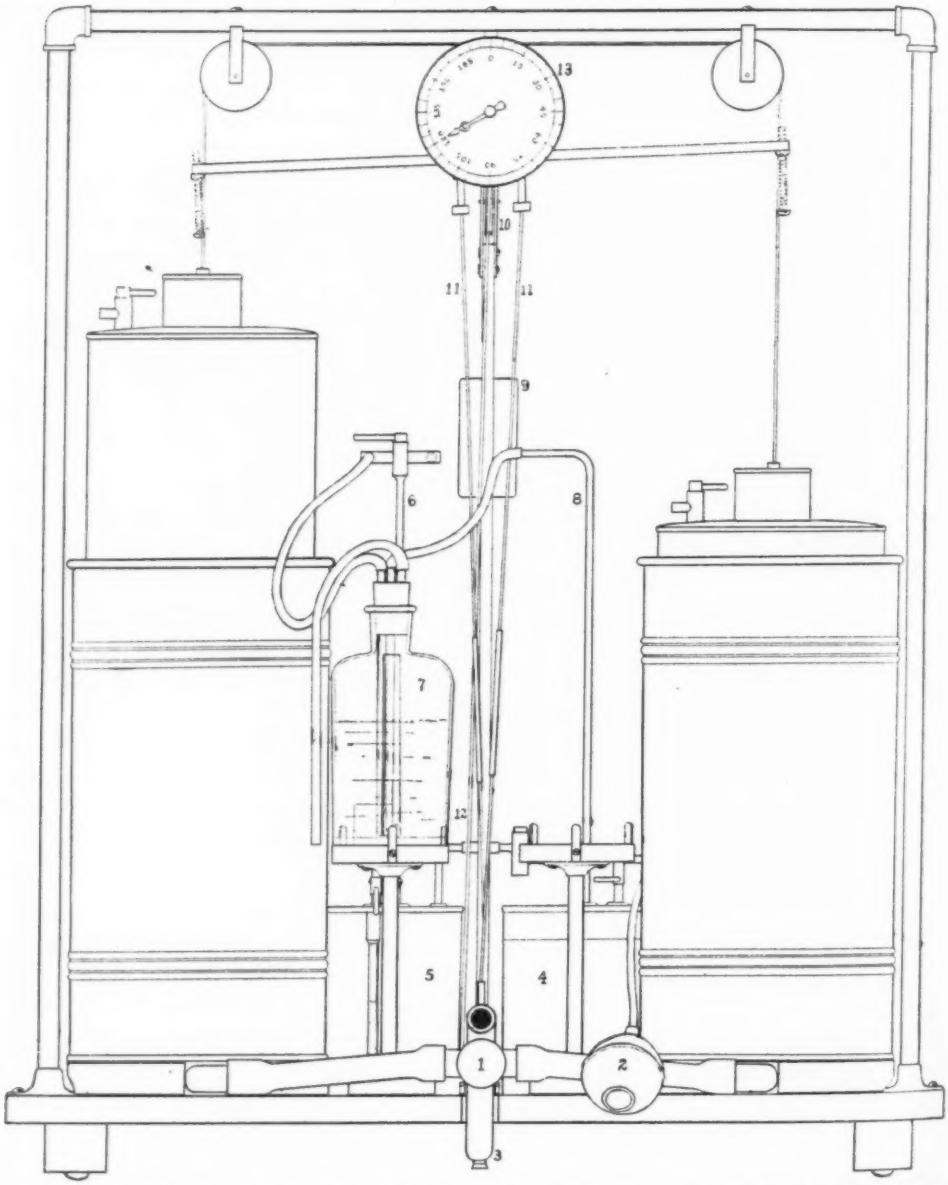


Fig. 1.—Spirometer, front view. (1) Four-way tap, with connection on shut-off tap to subject. (2) Air pump bulb. (3) Vent pipe for expired air. (4) Expired air reservoir and mixer. (5) Siphon reservoir. (6) Siphon. (7) Sample receiver. (8) Sampling tube. (9) Weight. (10) Weight pulley. (11) Trigger rods to controlling mechanism mounted behind the four-way tap. (Fig. 4.) (12) Cord from weight to driving windlass. (13) Dial.

back upon itself so the opening is directed upward. The opening is of such size that the siphon acting maximally, empties the bottle of water in about eight minutes. This tube is placed inside of a glass cylinder so that as air is drawn into the receiver, it passes to the upper part of the bottle through the cylinder, thus being limited in the extent of its contact with the mass of water in the bottle, and thus reducing loss of gases by absorption by water in case of unbalanced saturations, or partial pressures between the gases and liquid. The cylinder is of thin walled glass. The external diameter is slightly

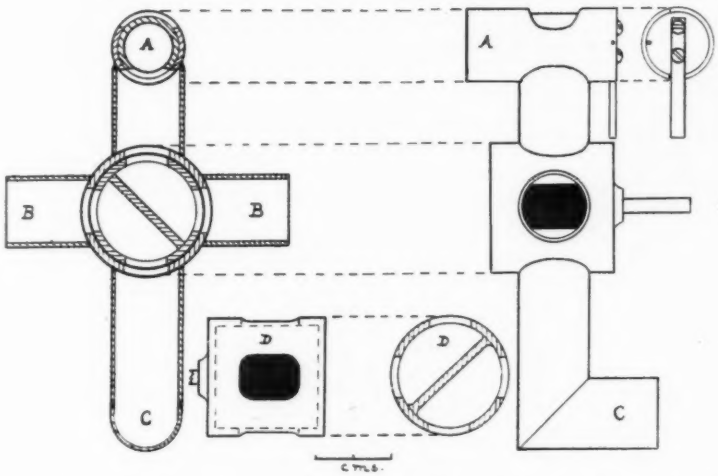


Fig. 2.—Four-way tap. *A.* Connection to subject *B.B.* Connections to spirometers. *C.* Outlet for expired air. *D.D.* Plug.

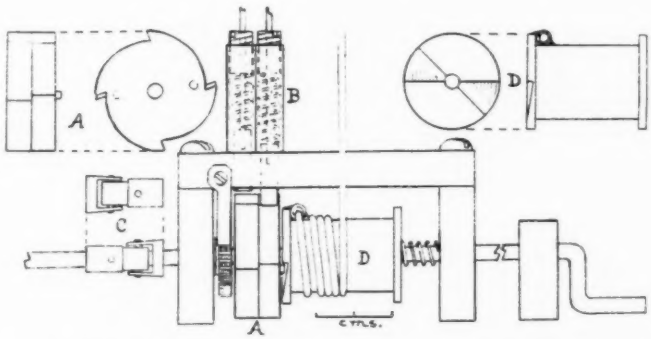


Fig 3.—Mechanism automatically turning four-way tap. *A.* Quadrant stop. *B.* Control triggers. *C.* Drive shaft to tap, and universal joint. *D.* Driving windlass with cord to weight

less than the narrowest internal diameter of the bottle neck. The lower end rests on the bottom of the bottle. The upper end extends to within one cm. of the lower opening of the bottle neck. The outer ends of the three tubes project about a cm. above the top of the stopper and are fitted with ten inch lengths of narrow bore, pure gum tubing for making connections.

To take a sample from the spirometer, the bottle is placed upon the holder and the siphon tube connected with the siphon. The subject is connected with the spirometer and expired air is pumped through both the siphon reservoir and through the siphon which is adjusted to the top of the reservoir and then

pumped through water in the receiver, the air being permitted to escape through the short inside tube of the receiver. When the water in the reservoir and the water in the receiver is saturated with the subject's expired air the vent tube of the receiver is closed and the third or pressure tube opened. The air pressure in the reservoir is then raised by pumping into it the subject's expired air which raises the pressure in the receiver until water is forced out through the third tube. The rubber connection on this tube is then

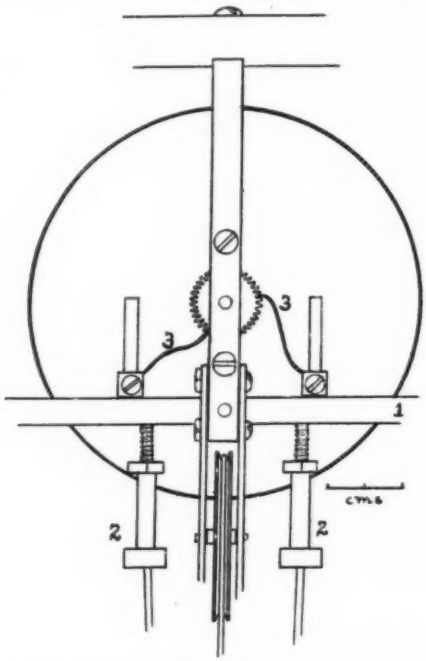


Fig. 4.—Back of dial. (1) Double horizontal lever. (2) Trigger rods. (3) Springs controlled by double horizontal lever so adjusted as to record on the dial each 5 liters of air introduced.

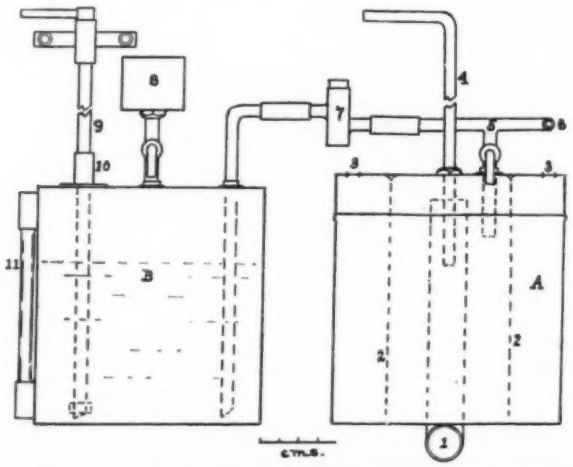


Fig. 5.—Showing details of: *A*, expired air reservoir and mixer; *B*, Siphon reservoir and connections. (1) Expiration tube from the spirometers. (2) Air baffle. (3) Vents for escape of air. (4) Sampling tube. (5) Tube for pumping expired air to siphon reservoir. (6) Pump connection. (7) Check valve on air line. (8) Filling cup and pressure equalizing vent. (9) Siphon. (10) Collar in which siphon slides. (11) Water gauge.

clamped near the end and attached to the sampling tube of the spirometer. The short inside tube or vent tube is now opened, the siphon pushed downward to the bottom of the reservoir, and the subject's expired air pumped into the reservoir, thus compressing the air and forcing the water into the re-

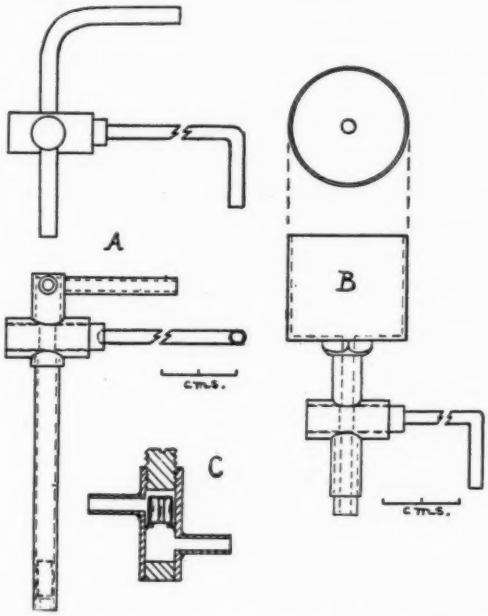


Fig. 6.—*A*, Top and side views of air connection for pumping expired air into siphon reservoir. *B*, Filling cup and pressure vent in siphon reservoir. *C*, Check valve on air line.

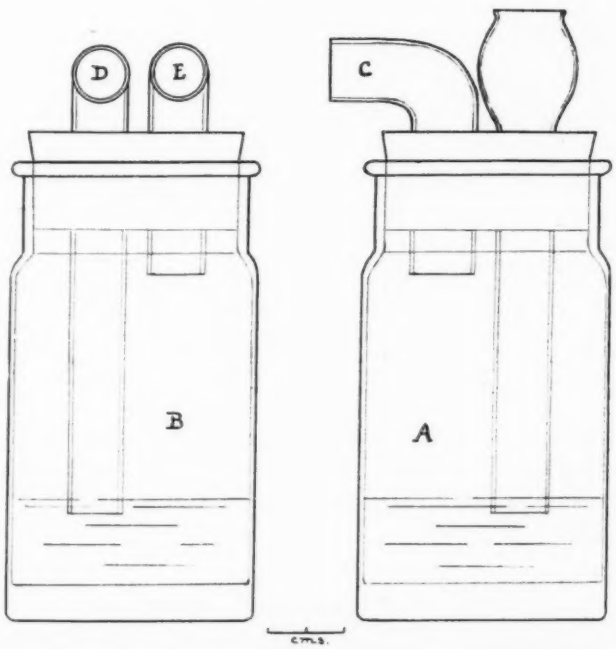


Fig. 7.—Water valves used with twin form of spirometer. *A*, Inspiration valve. *B*, Expiration valve. *A* rubber tube connects *C* with a *Y* to the stem of which a mouth piece is attached, and another rubber tube connects the other limb of the *Y* to *D*. *E* is connected to the spirometer tap.

ceiver. When this is completely filled with water, the vent tube is clamped near the outer end and the tap on the top of the reservoir opened to release the pressure and the siphon tube pulled upward until its lower end is checked by a stop just below the inner surface of the reservoir. The subject breathes continuously through the spirometer during this entire period which ensures that all air used for saturation purposes and that all air in the connections, i.e., the small quantity contained in the spirometer sampling tubes, is the subject's expired air.

The spirometer dial is now read for zero, the time noted and the clip on the sampling tube of the receiver removed. This starts the siphon and air is drawn from the expired air chamber of the spirometer into the receiver. When the observation is completed the time is noted, the dial read for total quantity of gas, and both the siphon and sampling tubes of the receiver are clamped near their ends and disconnected. The receiver is now ready for transferring to the holder used in connection with analyzing the sample.

To transfer samples to a gas burette the end of the siphon tube is connected with a displacing reservoir, as described elsewhere.[2]

## RESULTS

Basal metabolism results for man by this form of spirometer compared to the Tissot form are shown by the following experiment. Prior to the first test the individual reclined at rest for thirty minutes.

TABLE I

Results of successive tests of oxygen consumption for ten-minute periods by a Tissot and the Twin form of spirometer. Five to ten minutes elapsed between successive tests but the subjects in each group of observations remained quiet throughout the entire period. Water valves were used in all the tests. (Fig. 7.)

| DATE | STATE | FORM | TOTAL EXPIRED AIR | CARBON DIOXIDE PER CENT | OXYGEN PER CENT | RESPIRATORY QUOTIENT | BASAL RATE |
|---|---|---|---|---|---|---|---|
| 1921 | | | | | | | |
| April 21. | Not fasting. | Tissot | 47.23 L. | 4.094 | 15.897 | 0.773 | +9.64 |
| " 21. | " " | Twin | 42.58 | 3.999 | 15.753 | 0.723 | +1.87 |
| " 21. | " " | Tissot | 45.26 | 4.404 | 15.853 | 0.836 | +6.44 |
| " 22. | " " | Tissot | 57.00 | 4.216 | 16.066 | 0.834 | +13.89 |
| " 22. | " " | Twin | 53.72 | 4.025 | 16.183 | 0.812 | +4.75 |
| " 22. | " " | Tissot | 52.00 | 4.316 | 15.941 | 0.833 | +6.49 |
| " 23. | Fasting | Tissot | 44.40 | 4.233 | 15.817 | 0.787 | -10.08 |
| " 23. | " | Twin | 42.786 | 4.208 | 15.733 | 0.766 | -11.98 |
| " 23. | " | Tissot | 48.10 | 4.425 | 15.875 | 0.843 | -3.71 |

## SUMMARY

A form of spirometer for continuously and automatically measuring and sampling expired air is described. It was designed primarily for comparative experimental studies on laboratory animals to give results accurate to within about five per cent.

## REFERENCES

[1]Jour. Am. Med. Assn., April 6, 1907, xlviii, 1183.
Jour. Am. Med. Assn., September 9, 1911, lvii, 887.
Jour. Am. Med. Assn., October 27, 1917, lxix, 1394.
[2]Jour. Biol. Chem., Oct., 1921, xlviii, 373.

# A NOTE UPON THE UTILIZATION OF THE COMPLEMENT-FIXATION REACTION IN THE DIAGNOSIS OF TUBERCULOUS MENINGITIS*

By Robert A. Kilduffe, A.M., M.D., Pittsburgh, Pa.

With the exception of the meningococcus, the tubercle bacillus is probably the organism most frequently concerned in the production of acute inflammatory reactions in the meninges and, while in all probability, every case is secondary to some primary focus, this is often most difficult to find and, not infrequently, may not be demonstrable.

At autopsy the gross pathology varies within wide limits and may be represented only by lesions barely visible to the naked eye. It is not remarkable, therefore, to find that the results of laboratory examinations of the spinal fluid are also variable and that the diagnosis is often to be made only by exclusion.

As a general rule, the pressure of the cerebrospinal fluid is increased, though this is by no means invariably so, even a normal pressure being not incompatible with the disease. Lack of marked turbidity, a clear, limpid fluid, is a more constant finding but not characteristic of this condition alone, while the formation of a fibrinous, veil-like coagulum in the fluid on standing is highly characteristic though not pathognomonic. The cell count and globulin are both increased, the cytology being characterized by a perceptible and even marked increase in the number of small mononuclear lymphocytes; but, again, these findings, while fairly constant, are only suggestive.

The only absolute method of laboratory diagnosis is the actual demonstration of the tubercle bacillus, a procedure entailing many difficulties and offering varying chances of success—from 50 per cent to 100 per cent according to the method employed and the time consumed in the search. With animal inoculation, even in guinea-pigs previously x-rayed to reduce resistance, ten days is the earliest period in which conclusive results may be hoped for.

Kasahara[1] examines the spinal fluid before and after the intraspinous injection of 0.01 to 0.002 mg. of Old Tuberculin diluted to 1 c.c. with normal saline and, in five cases with three controls, reports, after injection, a marked increase in the number of polymorphonuclear and small mononuclear leukocytes together with, what he considers characteristic, a large number of erythrocytes; but these results have not been corroborated.

The infection, therefore, illustrates in a striking way the necessity for a close correlation between laboratory and clinical findings and is an example of the method of diagnosis by exclusion.

In the case herewith reported, because of the absence of any pathognomonic findings, a tuberculous complement-fixation test was made upon the

*From the Laboratories of the Pittsburgh Hospital.
Received for publication, July 28, 1921.

spinal fluid and upon the blood serum and conclusions based upon the following premises:

If the reaction occurred in the spinal fluid, the antigen being biologically specific, the positive reaction would indicate the presence of specific antibodies without, however, indicating their possible source. If, however, the reaction was negative in the blood serum, knowing that the interchange of antibodies between the blood and spinal fluid occurred only in slight degree, then it seemed fair to conclude that the positive reaction in the spinal fluid rose from the presence of tuberculous infection in the meninges. A positive serum reaction would as greatly diminish the significance of a positive spinal fluid reaction as a negative serum reaction enhanced it.

The method was, therefore, tried with successful results in the case reported and the report is made because of the absence of any note in the available literature concerning this method of laboratory diagnosis in tuberculous meningitis.

It is, of course, conceivable that the utility of the method will, in large measure, be determined by the antigen used and the duration of the infection, but it seems worthy of trial in the dubious case, at least.

The antigen used in this case was that supplied by Parke, Davis & Co.; complement being used in two units titrated plain with water-bath incubation at 38° C.

CASE REPORT

Mrs. M. F., No. 1319-21, aged forty-four, was admitted to the Pittsburgh Hospital April 18th, 1921, on the service of Drs. Wesley and Williams.

*Chief Complaint.*—Coma.

*Present Illness.*—For several months previous to admission the patient has had severe headaches, the localization of which is not well defined because of the necessity of obtaining most of the history from relatives. These have been accompanied by marked "nervousness." During the attacks she would have crying spells without apparent cause.

The day previous to admission she developed a headache of greater intensity than ever before, became dizzy, and complained that things "became black" before her. She partly recovered from this attack but, at 12.30 A. M. she screamed out, saying that her left side was becoming paralyzed and that she was going to die, and became unconscious, in which condition she was brought to the hospital.

*Past Medical History.*—No illness except measles in childhood.

*Family History.*—Married ten years; one living child. During the "past few years" has been in close attendance upon her husband who recently died from pulmonary tuberculosis, of which there is some family history.

*Physical Examination.*—Face much flushed; pupils pinpoint and slightly oval in shape; equal in size. Some evidence of mastoid tenderness increased on pressure. Patient is mentally fogged, with rambling speech, and generally lies in a comatose condition from which she can be aroused to some extent. In the past 24 hours has vomited frequently, which condition has now subsided. Knee-jerks increased; Babinski and ankle-clonus absent. When aroused complains of severe and agonizing frontal headache.

Heart shows nothing of marked importance. Some tenderness over left kidney on deep palpation; slight tenderness on deep palpation in right iliac region and also in hypogastric region where a small mass is palpable. Tenderness in lumbar region over area corresponding to both kidneys.

April 18, 19, and 20.—Constant headache and rambling delirium. Eye-grounds examined by Dr. Jennings. Negative.

April 23.—Consultation Dr. A. R. Matheny: No evidence of brain-tumor. Diagnosis: Tuberculous meningitis.

April 27.—Examined by Dr. Wright. Diagnosis: Cerebrospinal meningitis, subacute type, most likely tuberculous.

The patient's condition became progressively worse with deepening coma until death on May 10th. Autopsy refused.

*Laboratory Examinations.*—April 18.—Urine negative. Blood: Hb. 80 per cent. RBC: 5,200,000; WBC 19,600. Poly. 80 per cent; L.M. 6 per cent; S.M. 13 per cent; Eo. 1 per cent.

April 19.—Spinal fluid: Bloody; pressure normal. Presence of blood prevented cell count, globulin estimation and gold-sol test. B. tuberculosis not demonstrated.

April 21.—WBC 12,000. Blood Wassermann; negative (Cholesterinized extract human heart; acetone-insoluble lipoids human heart; alcoholic extract luetic liver).

April 23.—Spinal fluid: Bloody; pressure increased. Wassermann negative in 1 c.c. (triple antigen battery).

April 26.—Urine: trace of albumin; otherwise negative.

May 3.—Spinal fluid: Slightly cloudly fluid under increased pressure. Cell count, 300 per c.mm. Globulin increased. Lange colloidal gold reaction. 1100000000. Wassermann negative. B. tuberculosis not found. Tuberculosis complement-fixation test positive in 1 c.c.

May 4.—Blood serum: tuberculosis complement-fixation test negative in 0.2 c.c.

At no time was the tubercle bacillus demonstrated in the spinal fluid.

The report of this case is made possible through the courtesy of Drs. Wesley and Williams and is illustrative of a possible method of laboratory diagnosis in a condition often presenting a puzzling problem concerning which no mention is found in the current literature of the disease.

## REFERENCE

[1]Kasahara: quoted by Boyd, W.: The Physiology and Pathology of the Cerebrospinal Fluid, 1920, The MacMillan Co., ed. i, p. 100.

# CHAIR FOR PERFORMING SPINAL PUNCTURES*

By Thomas B. Christian, M.D., Morris Plains, N. J.

IN performing spinal punctures in insane patients it is quite different from that of performing spinal punctures among the sane. Most of them do not understand the reason for such procedure and will not cooperate. On account of the resistance it is rather difficult to gain entrance to the spinal canal and when you force an entrance a certain amount of damage is done and the fluid obtained is many times bloody. In different state institutions various methods are used, as putting the patients crosswise on tables, at foot of beds, and

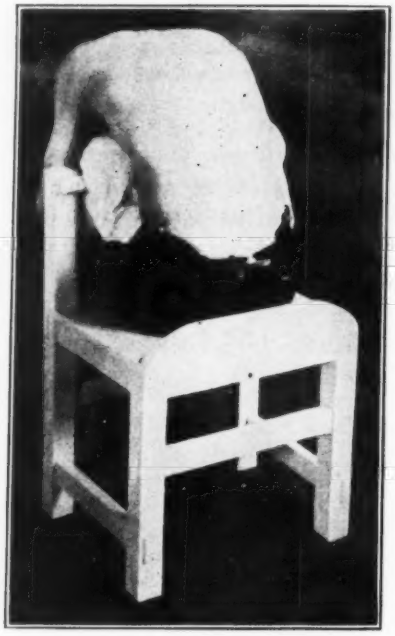

Fig. 1.

sideways in chairs, but this requires too many attendants to hold the resistive patients. We use a chair which is a very simple arrangement and it has the advantages in that only one attendant is required—can be used with the most violent case—and by holding the patient in the right position it diminishes the pain and clear fluids are obtained for examination. As shown in the illustration it is a plain, heavy-made chair with a small elevation in the back to keep the patient from sliding backwards and yet not high enough to interfere with working. The front consists of two heavy posts with a strong

*From the New Jersey State Hospital at Morris Plains.
Received for publication, August 8, 1921.

sliding rod. When the patient is seated push the rod down and over it place a pillow and the patient will find it very comfortable to bend over the rod. If the patient is violent a padded strap under his knees and over his neck will keep him in the correct position and it will be impossible for him to interfere with the spinal puncture. With this chair the following advantages have been found, the patient suffers less, painless after-effects diminished, less time consumed, less help required, used with violent cases and clear fluids obtained.

---

## DEVICES TO ELIMINATE CERTAIN OBJECTIONABLE FACTORS IN THE ANALYSIS OF GASTRIC CONTENT*

By J. L. Butsch, M.D., and Claire M. O'Brien, A.C., Buffalo, N. Y.

THE ordinary asbestos piston syringe has some objections, the most important of which are: It is not air tight and does not produce a good vacuum. The plunger must be moistened and in this way dilutes the gastric contents. The piston soaks up about 3 grams of water on an average, and since the specimen collected is usually 5 to 10 c.c. this makes an appreciable

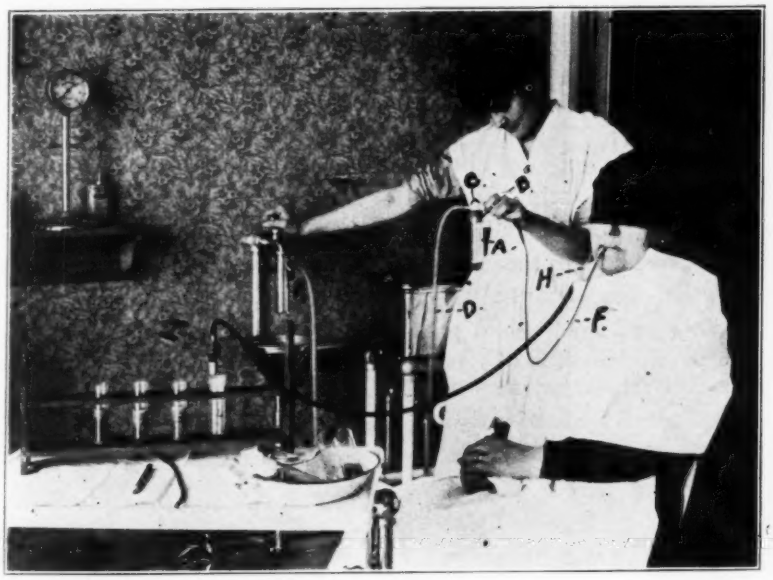


Fig. 1.

difference in the acidity per cent. Where a great many estimations are made the expense of the syringe is a factor. The aspirator method can be done more quickly and there is no necessity for the repeated sterilization of the syringes.

*Procedure.*—An ordinary salt mouthed bottle (*A*) is fitted with a two-hole

*Received for publication, August 11, 1921.

rubber cork (*B*) from which pass two glass tubes (*C*) bent at right angles. To one is attached a rubber tube (*D*) which connects it with an ordinary aspirator (*E*), and the other is connected with the sterile Rehfus tube (*F*) which has been introduced by the usual technic. After the tube has been introduced and the connection made, the water tap is turned on and the stomach contents readily flow into the collecting bottle. To collect the second specimen, all that is necessary is to place a fresh bottle onto the cork.

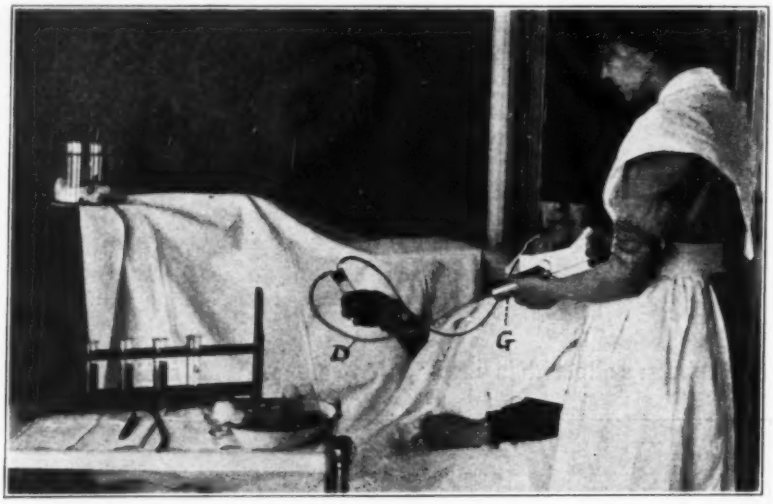


Fig. 2.

The same result may be obtained by connecting a large metal piston syringe (*G*) to the aspirating tube (*D*). To another aspirator (*I*) is attached a curved hook (*H*), on the end of which is a bulb with rather large perforations. This device keeps the excess saliva aspirated away, and there is no occasion for the constant swallowing of the saliva—which also dilutes the gastric contents and neutralizes part of the acidity. By using both devices greater accuracy in check reading is obtained.

# The Journal of Laboratory and Clinical Medicine

VOL. VII. APRIL, 1922 No. 7



Editor-in-Chief: VICTOR C. VAUGHAN, M.D.
Washington, D. C.

ASSOCIATE EDITORS

DENNIS E. JACKSON, M.D. - - CINCINNATI
HANS ZINSSER, M.D. - - - NEW YORK
PAUL G. WOOLLEY, M.D. - - DETROIT
FREDERICK P. GAY, M.D. - - BERKELEY, CAL.
J. J. R. MACLEOD, M.B. - - - TORONTO
ROY G. PEARCE, M.D. - - AKRON, OHIO
W. C. MACCARTY, M.D. - ROCHESTER, MINN.
GERALD B. WEBB, M.D. - COLORADO SPRINGS
WARREN T. VAUGHAN, M.D. - RICHMOND, VA.
VICTOR C. MYERS, PH.D. - - NEW YORK



Contents of this Journal Copyright, 1921, by The C. V. Mosby Company—All Rights Reserved


Entered at the Post Office at St. Louis, Mo., as Second-Class Matter


## EDITORIALS

### *Treatment of Denervated Muscle*

DURING the past few years investigations have been carried on in England and Canada which seriously question the value of electricity and massage in the treatment of denervated muscle. The beneficial effects of such treatment in normal muscle had led to the assumption of a like benefit in denervated muscle. But a denervated muscle, until the connecting of regenerated nerve fibers with the muscle fibers, is probably overactive, judging from the fibrillation which takes place. The discovery of fibrillation should have exploded the old disuse theory as the explanation of denervated muscle atrophy. But it was some time before the old attitude was changed. A normal muscle and a denervated muscle are distinctly different. While the former can be made to atrophy by disuse the latter atrophies apparently from excessive activity. In any consideration of treatment this distinction cannot be emphasized too strongly.

The only experimental work which had been done to test the value of treatment in denervated muscle up to 1915 was that of Reid and that of

Brown-Séquard, both in 1841. These experiments were so few and so incomplete that they established nothing.

Beginning in 1915 Langley and his collaborators in England made a careful study of the effect of massage and of electricity on the atrophy of denervated muscle. After bilateral denervation (popliteal nerves cut) lasting three weeks with treatment on one side, the differences in weights of corresponding muscles were nearly the same as in normal animals. They compared seven or eight muscle groups. The effects of condenser currents, passive movements and massage were tried in different animals. Their results showed no definite effect of treatment. In the conclusion the following statement is made:

"The general impression which we get from our experiments is that none of the methods of treatment of denervated muscle now in use—passage of galvanic current, production of contraction, passive movements and massage—can have more than a slight effect in delaying muscle atrophy."

The effect of treatment in denervated muscle was also studied by Hartman, Blatz and Kilborn. A large number of animals were used so that chance variation might be more easily ruled out. In all animals the contractile power of the muscles was used as a test in order to avoid the connective tissue factor which one does not rule out by a comparison of weights.

In the first series 37 rabbits were used, the soleus, gastrocnemius and plantaris muscles being denervated on both sides. The muscles of the right side were massaged from two to ten minutes a day over periods varying from seven to 190 days. Massage in this and all other series was performed by trained military masseuses. At the conclusion of the experiment the animal was anesthetized and the work capacity of the two sets of muscles compared. The massaged muscles were stronger than the controls in 62 per cent of the animals, but not knowing the relative powers of the muscles to begin with, the results were inconclusive.

A second series was studied in which the contractile powers of the muscles of the treated and untreated sides were tested at frequent intervals before and after denervation. Massage was employed in 58 rabbits and galvanic stimulation in 24 rabbits. These animals were observed for periods ranging from one to nine months. In those in which denervation had been produced by crushing the nerve, there was a return of function long before the termination of the observations. Neither massage nor galvanic stimulation hindered the loss of contractile power nor hastened its recovery when it began to return.

Finally a series of 125 animals was studied in which the ends of the severed tibial nerves were separated in order to check regeneration for periods of time ranging from one to seven months. At the end of this period the two ends were freshened and brought together by suture. The power of the gastrocnemii groups of the two sides was tested at frequent intervals. The denervated muscle group on one side was treated daily by either a slowly surging galvanic current or by massage. Here again neither massage nor electrical treatment appeared to benefit the denervated muscle.

From a study of more than 240 animals and many of these for over a

period of six months Hartman and Blatz conclude that massage and galvanic treatment in denervated muscle are futile.

A certain amount of passive movement is certainly necessary to prevent the development of adhesions but beyond that perhaps the best treatment is rest. In later stages of denervation when the circulation is diminished, hot baths may possibly be of some benefit by increasing the blood supply.

Until we know how to check fibrillation we shall probably not be able to prevent the atrophy of denervation. Neither massage nor electric currents do this except very briefly, therefore it is not surprising that they cannot be shown to be of value.

Still these forms of treatment might be useful after regeneration of the nerve fibers but so far as we know no one has ever been able to show that they delay the muscular atrophy due to denervation.

BIBLIOGRAPHY

Brown-Séquard: Compt. rend. Soc. de biol., 1841, p. 195.
Hartman and Blatz: Jour. Physiol., 1920, liii, 290. Ibid., 1921, liv, 392. Jour. Am. Med. Assn., 1920, lxxiv, 878.
Hartman, Blatz and Kilborn: Jour. Physiol., 1919, liii, 92.
Langley: Jour. Physiol., 1916, l, 335.
Langley and Hashimoto: Jour. Physiol., 1918, lii, 15.
Langley and Kato: Jour. Physiol., 1915, xl, 432.
Reid, John: Edinburgh Month. Jour. Med. Sc., May, 1841.

—*F. A. H.*

## *Carotinemia*

BY carotinemia is meant a condition of pseudojaundice which is characterized by the presence of carotin in the blood and certain tissues. It differs from jaundice in that bile is absent from the secretions and from the blood, and in that the characteristic discoloration does not affect the scleræ. The palms of the hands, soles of the feet, and nasolabial folds, cheeks and forehead are according to some reports, more apt to be pigmented. The color is most brilliant in well nourished persons, presumably because the pigment is soluble in fat. When the articles of diet in which the pigment occurs are eliminated from the diet, the color of the patient returns to normal. It seems certain that the xanthosis-diabetica is in fact carotinemia.

Carotin is a yellow pigment belonging with the xanthophylls in the group of carotinoids. To these substances is due the yellow color of cream, of egg yolk, and of corpora lutea. Under different circumstances the pigments are called lipochromes or lutein. They appear in many vegetables, especially in spinach, lettuce, oranges and carrots. Palmer has made a comprehensive study of carotinoids, and with his associates has demonstrated that the natural pigment of egg yolk, body fat and blood serum is physiologically identical with carotin; that the coloring matter of milk fat, body fat, skin secretions, corpus luteum and blood serum of the cow is also due to the same group of substances. They were able to produce milk fat and egg yolk almost lacking in yellow by

feeding diets poor in the respectively characteristic pigments. In the cow the carotin was in excess; in hens the xanthophylls predominated.

In 1919 Hess and Meyers described cases in which there was a peculiar yellow discoloration of the skin and in which carotin was present in the blood. These cases were children who had been fed on a diet containing carrots.

During the war when food shortage necessitated a more largely vegetarian diet, articles appeared in the German journals describing children with yellowish pigmentation. These children regained a normal color when carrots were removed from the diet. Diabetics fed upon food with high lipochrome content have been observed to develop xanthosis. In the vegetable foods used, and in eggs carotin has been found in excess of xanthophylls.

Most recently Head and Johnson have reported a case of carotinemia in an adult who gave carrots an important place in his diet. In the blood serum of this patient carotin was found to amount to approximately 0.00057 gm. per 100 c. c. of blood. Removal of carrots from the diet was followed by an almost complete return to normal color at the end of two months.

Carotinemia is probably commoner than is generally suspected. It is perhaps true that many cases called jaundice, especially ones which appear in persons who prefer a diet composed largely of vegetables, are in reality due to pigments of the carotinoid group. Cases of yellow pigmentation which do not affect the scleræ, in which the color is most intense in the palms of the hands, and in which bile is absent from the urine, should be looked upon with suspicion and studied with reference to their diet.

REFERENCES

Head and Johnson: Arch. Int. Med., 1921, xxviii, 268.
Hess and Myers: Jour. Am. Med. Assn., 1919, lxxiii, 1743.

—*P. G. W.*

---

## *What are Russia's Medical Needs?*

WE have received from the "American Medical Aid for Russia" a request to join in an appeal to the physicians of this country for medical aid in Russia. Naturally, one is sympathetic with requests of this kind and is inclined without question to accept such an invitation. In this case, however, there are certain things about which we think inquiry should be made.

We understand that the U. S. War Department has turned over to the American Relief Association $4,000,000 worth of medical supplies for distribution in Russia. We are told by an official of the American Relief Association that forty cars of these supplies went into Russia in October, 1921, and from the same informant, we learn that recently $150,000 worth of laboratory equipment went into Russia. We have in our hands a report on the health situation in Russia made by a committee sent by the League of Nations to Russia, with a statement of affairs up to January, 1922. In this report we are informed that the epidemic of cholera which became so threatening along the Volga has been

arrested, or at least has come to a standstill, in its westward progress. The report says: "The difficult transport situation in Russia assists in the localization of epidemics. Had railway traffic been normal, cholera would have spread westwards. It is surprising, however, that in spite of a fair traffic on the Volga the epidemic does not seem to have traveled very far by this route."

The report says that, according to Professor Tarassevitch, "not a single case of plague has been discovered within the frontiers of European Russia. There have been many suspected cases and all that came to the knowledge of the central or local health authorities were investigated by competent bacteriologists. Just outside European Russia, at Batum in the Caucasus, there was a definite focus of bubonic plague in 1920 with a case mortality of thirty-two per cent. A quarantine station was organized at Irkutsk, and flying laboratories were held in readiness at Moscow, Sebastopol, Saratov, Odessa and Tashkent."

The Health Committee of the League of Nations estimates that there have been 20,000,000 cases of typhus fever in Russia during 1920 and 1921, and it appears that this and relapsing fever have been and continue to be the most threatening epidemic dangers in Russia. There have been local epidemics of dysentery and in some provinces the death rate from this disease, especially among children, has been high. The malarial area in Russia has apparently been greatly extended and is said now to include Archangel. The Russian health authorities, we are told, have no great fear of an extensive outbreak of smallpox.

In this appeal by the "American Medical Aid for Russia," it is said that the intention is to ask for the equipment of an American hospital in Moscow. The report of the Health Committee of the League of Nations contains the following statement: "Nothing struck us so much as the exemplary cleanliness of a big municipal hospital in Moscow (Soldatenkov) which seemed an oasis amidst a desert of rubbish and untidiness surrounding it. All the plant of the hospital was in perfect working order and, in fact, working at full pressure, while the purely professional side seemed to be at a very high level. The staff which has succeeded in keeping this institution in such a state of preservation was being paid salaries much below the famine level, the nurses being paid 5,000 roubles per month and given their food only every second day. The situation of these nurses will be accurately appreciated if it is realized that a cake of soap in a Moscow shop costs 8,500 roubles."

So far as laboratory work and laboratory equipment are concerned, the League of Nations report contains the following paragraph: "In spite of such conditions of life, scientific activity in Russia has not ceased. In fact, one may say that the Russians are perhaps overdoing themselves in their zeal for establishing laboratories everywhere. In Moscow alone there appear to be twelve municipal bacteriologic laboratories, and in the Moscow district there are as many as thirty, while the output of these institutions as regards production of vaccine and serum is rather meagre and the staff very numerous. And yet the scientific researches carried out throughout Russia would do justice to any country. Of course, they have not discovered finally the etiology of typhus. But who has? We should like particularly to mention that we visited a truly magnificent exhibition organized by the Municipal Food Analysis Laboratory

in Moscow, an exhibition which showed the various kinds of bread which have been used by the populations in the various districts of Russia since 1917."

The League of Nations report gives the following statement, which may be of interest: "We have naturally inquired into the needs of the Russian Central Administration. We were given to understand that they were in no need of foreign medical personnel—interpreters would have to be attached to foreign sanitary units whose range of activity was thus rather limited. The People's Commissary of Health did not emphasize the necessity for very large quantities of hospital equipment. He informed us that he could rely on having 125,000 epidemic beds within the frontiers of Soviet Russia, and, in fact, it seems that Russia is at present under better conditions as regards hospital equipment than Poland was in the winter of 1919. This is explained by the fact that large supplies of military hospital stores fell into the hands of the Red Armies after the collapse of Koltchak, Denikin, Wrangel, etc. There is, however, a very great dearth of drugs of practically every kind. Quinine is almost unobtainable, and this at a time when malaria has been spreading at a very alarming rate. There is also a great scarcity of essential instruments such as syringes, etc. There is also room for an almost unlimited supply of soap."

With this more or less contradictory evidence before us, we can only ask, What is the truth about the sanitary condition in Russia?

—*V. C. V.*